ORGANIC CHEMISTRY
FOR
ADVANCED STUDENTS

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PART I

REACTIONS

BY

JULIUS B. COHEN, PH.D., B.Sc., F.R.S.

PROFESSOR OF ORGANIC CHEMISTRY IN THE UNIVERSITY OF LEEDS

THIRD EDITION

LONDON

EDWARD ARNOLD

41 & 43 MADDOX STREET, BOND STREET, W.

1920

PRINTED AT OXFORD, ENGLAND
BY FREDERICK HALL
PRINTER TO THE UNIVERSITY

PREFACE TO THE SECOND EDITION

The object of recasting the former two volumes of the 'Organic Chemistry for Advanced Students' in the three parts in which they now appear has been to group together allied subjects and to link them as far as possible in a consecutive form. As this entailed re-arrangement of the plates, an opportunity was afforded of bringing the subject-matter up to date, and very considerable additions have been made to the contents of the former volumes. As stated in the original preface, the book is not intended to serve as a reference book, but to furnish a general survey of those fundamental principles which underlie the modern developments of this branch of chemistry.

J. B. COHEN.

March, 1918.

PREFACE TO THE THIRD EDITION

Advantage has been taken of the necessity for a reprint to add a number of references to recent literature, which will enable the student to bring his information up to date.

J. B. COHEN.

July, 1920.

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ORGANIC CHEMISTRY

PART I

CHAPTER 1

HISTORICAL INTRODUCTION

The Radical[1] of Benzoic Acid. In the year 1832 Liebig and Wöhler published their classical memoir, entitled, 'Experiments on the Radical of Benzoic Acid'.[2]

Viewed in the light of our present knowledge there is nothing very remarkable in the facts which they discovered. Starting with bitter almond oil, which we now term *benzaldehyde*, they converted it by the action of chlorine and bromine into benzoyl chloride and bromide. Benzoyl chloride treated successively with potassium iodide gave benzoyl iodide; with ammonia, benzamide; with lead sulphide, benzoyl sulphide; with mercuric cyanide, benzoyl cyanide and with alcohol, benzoic ether. Bitter almond oil had, moreover, been found by Stange (1824) to undergo rapid oxidation in the air and to be transformed into an acid—benzoic acid—identical with the substance derived from gum benzoin.

Such is briefly the substance of the investigation to which the following introduction is attached. 'When a chemist is fortunate enough to perceive one ray of light penetrating the dark region of organic nature, which may mark the entrance to the right path of future knowledge, he has reason to feel encouraged, although conscious of the vastness of the field which lies before him.'

In order to realize the importance of a memoir which created a profound impression among contemporary chemists, and was welcomed by Berzelius as 'the dawn of a new day', we must take a glance at the branch of chemistry which at this period formed 'the dark region of organic nature'.

Origin of the Radical Theory. If we turn to Lemery's *Cours de Chymie*, which was the popular text-book from 1675 down to the middle of the eighteenth century, we find all known substances

[1] It is an interesting and curious fact that with admittedly 'little to recommend it' (*Trans. Chem. Soc.*, 1905, 87, 548) the Chemical Society of Great Britain has seen fit to alter the original spelling to 'radicle', and the Society now holds the unique position of being the only representative body of chemists which has adopted this spelling.

[2] Liebig's *Annalen*, 1832, 3, 249; Ostwald's *Klassiker*, No. 22.

distributed according to their origin between the mineral, vegetable and animal kingdoms. Under the two divisions of vegetables and animals occur the names of substances which have been known from remote times, such as sugar, starch, fats and oils, gums and resins. By the process of distillation alcohol had been obtained from fermented liquids, acetic acid from vinegar, turpentine from resin, and various sweet scented oils from plants. Vegetable colouring matters were employed in dyeing, and oils and fats in the production of soap. Extracts of cinchona bark, opium and other vegetable substances were used in medicine. Towards the close of the eighteenth century Scheele isolated and clearly distinguished the acid principles present in various vegetable and animal products. He found malic acid in apples, citric acid in lemons, oxalic acid in wood sorrel, gallic acid in galls, lactic acid in sour milk, and uric acid in urine. He also obtained from olive oil, by boiling it with lead oxide, a sweet, viscid liquid, which we now know as glycerine.

These varied products of animal and plant life which, when ignited took fire, or when heated in closed vessels charred and gave off water and other volatile matters, contained, according to the views of the phlogistonists, more of the aqueous and combustible principle or phlogiston, than mineral substances. They were termed *organic* to indicate their origin from living or organized matter.

With Lavoisier's discovery of the cause of oxidation and combustion, the element oxygen became in chemistry very much what the sun is in our solar system. The chemistry of Lavoisier was the chemistry of oxygen. All compounds were oxides, generally simple oxides of another element. To the other element attached to oxygen de Morveau applied the term *base* or *radical*. The simple oxides were divided into salifiable and acidifiable bases, and these united to form salts.[1] The system was essentially dualistic, and contained the germ of the theory subsequently developed by Berzelius. Lavoisier, who was the first to demonstrate the true composition of organic substances, extended the idea of radical so as to embrace these compounds (1784). Organic substances which generally contained carbon, hydrogen, and oxygen, and occasionally nitrogen and phosphorus, were regarded as oxides of a radical, composed of at least two elements, carbon and hydrogen. Sugar, which yielded oxalic acid on oxidation, was the oxide of a hydrocarbon radical, and oxalic acid formed its higher oxide. *The radical was purely hypothetical.* Indeed, so little was then known about the nature of organic compounds that, with the advent of the atomic theory,

[1] Lavoisier's *Elements of Chemistry*, translated by Kerr, 1802, I, 289.

it was held to be doubtful if the elements composing them combined in simple atomic proportion and obeyed the laws of combination which had been found to obtain in the province of inorganic chemistry. Organic compounds were the products of a *vital force*, not necessarily dependent on the chemical laws governing inert matter. This view was commonly held until Berzelius, in 1814, by improving the method of organic analysis, showed from the results of his analyses of sugar and some of the organic acids, that organic compounds were subject to the ordinary laws of chemical combination.

Berzelius adopted Lavoisier's view of the nature of organic compounds; for in his *Treatise on Chemistry* (2nd edition), published in 1817, he says: 'After having become more closely acquainted with the difference between the products of organic and inorganic Nature and the different manner in which their constituents are combined together, we have found the difference to consist in this: that in inorganic Nature all oxidised bodies possess a *simple radical*, whilst all organic substances consist of oxides of *compound radicals*. In vegetable substances the radical consists usually of carbon and hydrogen, and in animal products of carbon, hydrogen, and nitrogen.'

To follow the history of organic chemistry from this point, and to realize the network of difficulties in which its votaries became gradually and unconsciously entangled, it will be necessary to understand the electro-chemical system of Berzelius and the method of notation which was founded upon it.

The Atomic and Molecular Weights of Berzelius. The discovery, in 1808, of Gay Lussac's law governing gaseous combination or the 'law of volumes', as it was commonly called, of Dulong and Petit's law (1819) which determined the relation of specific heats to the combining weights of the elements, and of Mitscherlich's law of isomorphism (1820) enabled Berzelius, after a careful revision of the combining proportions of the elements, to assign atomic weights based upon principles which we still recognize and adopt. Thus, if equal volumes of elementary gases contain the same number of atoms, the formula for water must be represented by H_2O since two volumes of hydrogen unite with one volume of oxygen; NH_3 will stand for ammonia, and HCl for hydrochloric acid. The method did not involve any question as to the volumes occupied by the combined gas, which offered a difficulty only solved later when Avogadro's distinction of *molécules constituantes*, and *intégrantes*, or, as we now say, atoms and molecules, was clearly recognized.[1] The

[1] *Die Grundlagen der Molekulartheorie*, Ostwald's *Klassiker*, No. 8; *Avogadro and Dalton*, by A. N. Meldrum, Pub. W. F. Clay, Edin.

direct application of the law of volumes was limited to comparatively few elements. A wider range of atomic weights was derived from the specific heats of the metals and the isomorphism of their salts. Where none of these principles could be applied the atomic weights were ascertained by the simplest gravimetric relation of an element to oxygen in its oxide. The atomic weights of the metals which formed basic oxides were derived from those oxides which were assumed to contain a single atom of each element. Consequently the atomic weights of the alkali metals and of silver which formed isomorphous salts with them, received double their present values. The formulae for potassium and silver oxide and chloride were written KO, KCl_2, AgO, $AgCl_2$; the formulae of ammonia and hydrochloric acid, originally written NH_3 and HCl, were afterwards doubled by using the *barred* or double atom thus: $NH_3 = N_2H_6$ and $HCl = H_2Cl_2$ with the object of making them equivalent to the atomic weights of the metals. For the same reason H_2 was the equivalent of 1 atom of oxygen and the formula for water appeared as $HO = H_2O$.

The series of atomic weights elaborated by Berzelius with rare analytical skill and an unerring instinct, which guided him where principles failed, differ little from the modern values.

In the third column of the following table is a list of the more important atomic weights taken from Berzelius' revised numbers, which appeared in 1826, oxygen being 1·00. The fourth column contains the figures calculated with hydrogen as the unit; in the fifth column are the present values:

Name.	*Formula.*	*Berzelius' numbers.*		*Present numbers.*
		O = 100	H = 1	H = 1
Oxygen	O	100	16·026	15·88
Hydrogen	H	6·229	1·000	1·00
Nitrogen	N	88·518	14·186	13·93
Sulphur	S	201·165	32·239	31·83
Phosphorus	P	196·155	31·436	30·77
Chlorine	Cl	221·325	35·470	35·18
Iodine	I	768·781	123·206	125·90
Fluorine	F	116·900	18·734	18·90
Carbon	C	76·437	12·250	11·91
Potassium	K	489·916	78·515	38·86
Sodium	Na	290·897	46·620	22·88
Silver	Ag	1351·607	216·611	107·12
Calcium	Ca	256·019	41·030	39·80
Strontium	Sr	547·285	87·709	86·94
Barium	Ba	856·880	137·325	136·40
Iron	Fe	339·213	54·363	55·50
Aluminium	Al	171·167	27·431	26·90
Chromium	Cr	351·819	[illegible]5·383	51·70

In a memoir published in 1826, 'Sur quelques points de la théorie atomistique,' Dumas[1] attempted to extend the application of Avogadro's hypothesis to the determination of both atomic and molecular weights from the densities of gases and vapours, in connection with which he devised his well-known method. It is a curious fact that he not only failed to commend his method to the chemical world, but ended by convincing himself of its futility.

The result was due partly to a clumsy way of presenting his ideas, and partly to the confusion introduced by the anomalous vapour densities of some of the elements. Dumas set forth that equal volumes contain the same number of atoms or molecules; consequently, if one volume or atom of hydrogen unites with one volume or atom of chlorine to form two volumes or atoms of hydrochloric acid, the original atoms of hydrogen and chlorine are divisible into half atoms of each element. A half atom of oxygen must for the same reason be present in the atom of water and so forth. Though Dumas, no doubt, clearly distinguished between his physical atoms or molecules and his chemical or half atoms, the subdivision of the atom implied a contradiction in the term and did not fail to call forth criticism. As Dalton said, 'No man can split an atom.'[2]

But this was not all. Dumas' atomic weight for silicon, which he correctly interpreted from the vapour density of the chloride, differed from the number obtained by Berzelius, who derived it from the oxide, written SiO_3 from its analogy with SO_3, CrO_3, &c. The atomic weight of mercury, determined from the vapour density of the metal, was half that assigned by Berzelius from its specific heat. Finally, the anomalous vapour densities of phosphorus, sulphur, and, as Mitscherlich found later, arsenic, gave atomic weights which conflicted with those previously derived by Dumas himself from the vapour densities of their hydrides and chlorides and shook his confidence in his own method.

Berzelius' system of atomic weights also had its critics. As we have seen, doubt had been thrown by Dumas on the validity of the law of volumes. The atomic weights of several of the elements which were derived from the specific heats did not conform to the atomic weights deduced from the law of isomorphism; for example, the isomorphism of the silver salts and those of the alkalis fixed the atom of silver at 216, whilst its specific heat gave the number 108. Mitscherlich's law itself was not free from objection, inasmuch

[1] *Ann. Chim. Phys.*, 1826, 33, 337.
[2] *Memoirs of Dalton*, by Dr. Henry.

as the existence of dimorphous substances left the choice in some cases doubtful.

The principles which served Berzelius for his determinations gradually fell into discredit.

Gmelin's Equivalents. Leopold Gmelin, the author of the classical treatise which bears his name, suggested a reversion to the system of *equivalents*, a term introduced by Wollaston in 1808. It represented the simplest gravimetric relations, without reference to the law of volumes, and received strong support from Faraday's newly discovered electrolytic law (1832).

The old and new systems were easily reconciled by using the barred or double atom of Berzelius, and appeared side by side for many years without giving rise to confusion, until the double atom eventually disappeared. Kolbe was one of the last to use the barred atom of Berzelius, which he abandoned about 1850 in favour of the equivalent notation.

The following formulae for water, hydrochloric acid, ammonia, and phosphoric oxide, represent the original and modified notation of Berzelius and the corresponding equivalent notation of Gmelin:

Berzelius (H = 1 ; O = 16)	original formula	H_2O	H_2Cl_2	N_2H_6	P_2O_5
	modified "	H̶O	H̶Cl	N̶H̶$_3$	P̶O$_5$
Gmelin (H = 1 ; O = 8)	equivalent "	HO	HCl	NH_3	PO_5

Henceforth, densities of volatile organic compounds, though frequently determined with the object of controlling analytical results, never served as a means of ascertaining molecular weights until many years had elapsed, when Gerhardt and Laurent revived the hypothesis of Avogadro and Ampère. The aggregate weight of the atoms might correspond to one, two, or a multiple of two volumes of the vapour compared with one volume of hydrogen.

The formulae for chloral $C_4Cl_6H_2O_2$, chloroform $C_2H_2Cl_6$, alcohol $C_4H_{12}O_2$, and acetic ether $C_8H_{16}O_4$, corresponded to four volumes, whereas those for ether $C_4H_{10}O$, oxalic ether $C_6H_{10}O_4$, and succinic ether $C_8H_{14}O_4$, corresponded to only two volumes. It was left to the choice of the investigator to select an appropriate molecular formula. We shall presently see how the confusion, which arose from the absence of any recognized method for fixing molecular weights, resulted in many a fruitless and embittered controversy.

Berzelius' Electro-chemical Theory. The electro-chemical theory of Berzelius (1819) dominated chemistry during the first third of the

last century. Carefully elaborated in the case of inorganic compounds, it was sought to apply it in the same comprehensive manner to organic compounds. It was the guiding principle to which Berzelius clung throughout his life. But the young and rapidly growing branch of the science was not to be crippled by an artificial system which arrested its natural development. After a fierce controversy between Berzelius and the chemists of the French school the theory was finally abandoned. The theory may be briefly defined as Lavoisier's dualistic views expressed in the light of Davy's and Berzelius' electro-chemical researches. Each atom of the elements was supposed to possess opposite electrical poles provided with different quantities of electricity, so that it contained a surplus of one or other kind of electricity, and was either positive or negative according to the predominating polarity. It was by virtue of their opposite polarities that the atoms combined. The simple combinations of positive and negative elements furnished compounds of the *first order*. The electricities in these compounds were not necessarily neutralized, and there might still remain a surplus positive or negative charge which enabled them to enter into further combinations, forming compounds of the *second order*. The elements were arranged in electrical series with oxygen at one end, representing the most electro-negative element, and the alkali metals at the other, representing the most electro-positive elements. Each intermediate element would be electro-positive to the one that preceded and electro-negative to that which followed. The metals were strongly, the non-metals weakly electro-positive towards oxygen. The lower metallic oxides retained, therefore, a residual positive, the non-metallic oxides a residual negative polarity. Thus potash KO was electro-positive, whilst sulphuric acid SO_3 was electro-negative. Potash and sulphuric acid could therefore combine, by virtue of their opposite polarities, to form sulphate of potash, which was written $SO_3 + KO$. The electricities might still remain unneutralized, and by the formation of double salts such as potash alum, compounds of the *third order* were obtained.

The oxides of the non-metals were called acids; N_2O_5 stood for nitric acid and $N_2O_5 + H_2O$ was its hydrate. When the combined water of the hydrate or *basic water* was replaced by a metallic oxide or base, a neutral salt resulted. The same principle was applied to organic acids and their salts. Acetic acid was written $C_4H_6O_3$ and its hydrate (our acid) $C_4H_6O_3 + H_2O$; C_2O_3 stood for oxalic acid, and the crystalline compound which we now term anhydrous oxalic acid $C_2O_3 + H_2O$ was regarded as its hydrate; benzoic acid was $C_{14}H_{10}O_3$ and

its hydrate (our acid) was $C_{14}H_{10}O_3 + H_2O$. The molecular formula for the acids was derived from the composition of the salts, usually the silver salts, and as all salts were supposed to contain one atom of base (silver and the alkalis had double their present atomic weights), it necessarily followed that all monobasic acids, like acetic and benzoic, had double their present formulæ, whereas dibasic acids received their modern values. It should be observed that these so-called organic acids only existed in the form of their hydrates, the acids themselves being purely fictitious groups of elements.

Organic Chemistry in 1830. In 1830 Liebig introduced his new method of organic analysis, which is essentially the one we still employ.[1] There is no doubt that the simplicity and rapidity of this process gave a new impulse to the study of organic chemistry. To perform an organic analysis appears to have been a troublesome business, for in a letter from Wöhler to Liebig written in August, 1830, we read: 'A thousand thanks for your quick reply. To be able to complete an analysis so rapidly is scarcely within the power of any one but yourself, certainly not in mine, for I have a wholesome dread of doing one.'

Organic chemistry in 1830 embraced a large number of substances of widely different properties, yet composed usually of only three or four elements—carbon, hydrogen, oxygen, and nitrogen. It included a variety of organic acids and a steadily increasing number of organic bases or alkaloids, the first of which—morphium—had been isolated in 1817 by Sertürner from opium; also a number of indifferent substances—hydrocarbons, spirits of wine, sugar, starch, gums—and finally, the fats and fixed oils, the composition of which had been studied by Chevreul in so complete and masterly a fashion that our knowledge of these substances has not materially advanced since his day. He showed that these bodies were compounds of glycerine with various acids (the fatty acids) and that they behaved like acetic ether, decomposing with alkalis into the salt of the acid and glycerine. There was, however, little analogy between the complexity of all these bodies and the simple compounds of inorganic chemistry, in which one element united with another in one or two, more rarely in three, proportions. Berzelius[2] at first distinguished inorganic compounds as binary, that is to say, divisible and sub-divisible into two parts, one electro-positive and the other electro-negative, whilst organic compounds contained more than two elements which were

[1] Berzelius, *Jahresb.*, 1831, 11, 214; Pogg., *Ann.*, 1831, 21, 1.
[2] *Ann. Phil.*, 4, 323.

directly combined into a whole and could not be subdivided or reunited after the manner of inorganic compounds. Hydrocarbons like marsh gas and turpentine, since they contained only two elements, were consequently classed among inorganic compounds, and occur under this head in the earlier numbers of Berzelius' *Jahresbericht*. But this distinction was not long maintained. Organic chemistry was still essentially the chemistry of animal and plant products and their derivatives. It is true that from time to time the artificial production of natural substances was announced. As far back as 1776 Scheele had obtained oxalic acid identical with that in wood sorrel by the oxidation of sugar with nitric acid. In 1822 Döbereiner had prepared formic acid, hitherto obtained by the distillation of ants, by the oxidation of tartaric acid, and had also converted alcohol into acetic acid by the aid of platinum black. In 1826 Hennel had synthesized alcohol from olefiant gas.[1] Again, in 1828, Wöhler found that in attempting to obtain ammonium cyanate by the action of ammonium chloride upon silver cyanate, or ammonia on lead cyanate, a crystalline compound was formed which was identified as urea, a substance only previously found in urine. But none of these artificially prepared substances was entirely independent of an animal or vegetable origin. Even the cyanates were derived in the first instance from potassium ferrocyanide, in the preparation of which animal matter was employed. These facts did little to disturb the belief in a vital force. Both Döbereiner's and Wöhler's discoveries are referred to by Berzelius in his *Jahresbericht*,[2] but it is clear that the rare example of isomerism furnished by the conversion of ammonium cyanate into urea created a far deeper impression than the realization of this much quoted synthesis.

Before the year 1832 the only organic substance from which a number of simple derivatives had been obtained was alcohol. With sulphuric acid it was known to yield, according to the conditions of the experiment, sulphovinic acid, ether, olefiant gas and a substance known as *oil of wine* of the formula $(CH_2)_n$; with hydrochloric acid it gave hydrochloric ether; with nitric acid, nitric (nitrous) ether; with acetic acid, acetic ether, and with oxalic acid, oxalic ether. Further, the oil of the Dutch chemists, as it was called, was obtained by combining olefiant gas with chlorine, and Hennel showed that sulphovinic acid was formed by the union of olefiant gas and sulphuric acid.[3] The relationship of alcohol to its derivatives was a matter of general

[1] *Phil. Trans.*, 1826, 240; 1828, 365; Pogg., *Ann.*, 1827, 9, 21; 1828, 14, 282. See also *Chemical Synthesis of Vital Products*, p. 2, by R. Meldola, 1905.

[2] *Jahresb.*, 1823, 2, 160; 1829, 9, 266.

[3] Pogg., *Ann.*, 1828, 14, 273; *Phil. Trans.*, 1826, Pt. 2, 240.

speculation which had free play, since no recognized method for ascertaining molecular weights existed.

The Etherin Theory. In 1828 Dumas and Boullay[1] propounded a theory which was intended to show the relationship of these substances. It was based upon an observation of Gay-Lussac's that the vapour density of ether was equivalent to that of one volume of olefiant gas and half a volume of water vapour, whereas that of alcohol was equivalent to half a volume of olefiant gas and half a volume of water vapour. Dumas and Boullay regarded alcohol, ether, and all their derivatives as containing one common group of elements, olefiant gas, which had the formula $2C_2H_2$, corresponding to the modern C_2H_4 (the atomic weight of carbon was derived by Dumas from the vapour density of marsh gas and olefiant gas, which he wrote CH_2 and C_2H_2 respectively, giving the number 6 to carbon). To the central group Berzelius gave the name of *etherin*, by which he signified oil of wine and denoted it by the formula[2] C_4H_8, but the fundamental idea was the same in both, and the theory was henceforth known as the *etherin theory*.

In addition to presenting a series of related compounds as containing a common group or radical, it explained Hennel's preparation of sulphovinic acid from ethylene and sulphuric acid, the existence of oxamethane (oxamic ester) obtained by Dumas from oxalic ester and ammonia gas and the curious inflammable platinum organic compounds of Zeise, which the latter prepared by the action of alcohol on platinic chloride and which contained no oxygen.[3]

An essential part of Dumas and Boullay's theory was to institute a comparison between etherin and its derivatives and ammonia and its compounds, which were written as follows:

	Formulae of Dumas and Boullay.	*Formulae of Berzelius.*	*Ammonia and its Compounds.*
Olefiant gas	$2C_2H_2$	C_4H_8	N_2H_6
Hydrochloric ether	$2C_2H_2+HCl$	C_4H_8+2HCl	N_2H_6+2HCl
Ether	$4C_2H_2+H_2O$	$C_4H_8+H_2O$	$N_2H_6+H_2O$
Alcohol	$4C_2H_2+2H_2O$	$C_4H_8+2H_2O$	
Acetic ether	$4C_2H_2+C_8H_6O_3+H_2O$	$C_4H_8+C_4H_6O_3+H_2O$	$N_2H_6+C_4H_6O_3+H_2O$
Nitric ether	$4C_2H_2+N_2O_5+H_2O$	$C_4H_8+N_2O_5+H_2O$	$N_2H_6+N_2O_5+H_2O$
Oxalic ether	$4C_2H_2+C_4O_3+H_2O$	$C_4H_8+C_2O_3+H_2O$	$N_2H_6+C_2O_3+H_2O$
Oxamethane	$4C_2H_2+C_4O_3+NH_3$	$C_4H_8+C_2O_3+NH_3$	—
Sulphovinic acid	$4C_2H_2+2SO_3+2H_2O$	$C_4H_8+S_2O_6+2H_2O$	—
Zeise's compound	$4C_2H_2+2PtCl_2$	$C_4H_8+Pt_2Cl_4$	—

[1] *Ann. Chim. Phys.*, 1828, (2), 36, 294, (2), 37, 15.
[2] *Jahresb.*, 1832, 12, 303.
[3] *Annalen*, 1834, 9, 1.

Dumas and Boullay went so far as to state that olefiant gas, were it but soluble in water, would exhibit alkaline properties, and they even attempted to extend their theory so as to embrace compounds like the fats and oils, which were assumed to possess an imaginary hydrocarbon radical united to ether, and even the sugars which were described as carbonates of etherin. The theory found many supporters and long held its ground in France. Berzelius, on the other hand, gave it a half-hearted reception,[1] which soon changed to undisguised hostility. He pointed out that the existence of the radical C_4H_8 might be accepted as a mere matter of convenience, but that the formula for alcohol could be equally well represented by either $C_4H_8 + 2H_2O$ or $C_4H_{10}O + H_2O$. The fact of alcohol yielding olefiant gas was no more a reason for the presence of this group in alcohol than there was for the pre-existence of nitrous oxide in nitrate of ammonia merely because nitrous oxide was evolved on heating. If olefiant gas were alkaline, then surely alcohol and ether, which were soluble hydrates, should also have alkaline properties. Moreover, though olefiant gas could be prepared from alcohol, neither alcohol nor ether could be formed by the reverse process of adding water to olefiant gas, and the analogy with ammonia broke down.

Furnished with fresh weapons Berzelius returned to the attack in the following year.[2] Liebig and Wöhler had shown that sulphovinic acid had the formula $C_4H_8 + 2SO_3 + 2H_2O$, containing, therefore, two atoms (molecules) of basic water, yet it only saturated one atom of base, and consequently the remaining atom of water must be an integral part of the organic constituent, just as it was of ammonia in the sulphate $N_2H_8O + SO_3$.

Growth of the Radical Theory. We can now realize how matters stood when Liebig and Wöhler, in the memoir to which reference has been made, brought the first unassailable evidence of the existence of an organic compound radical. A series of substances had been obtained which were readily convertible into one another by simple reactions such as chemists were familiar with in inorganic chemistry. They contained one common group of elements $C_{14}H_{10}O_2$ to which the name *benzoyl* (*benz*, the root of benzoic. and ὕλη, substance) was given. The compounds were written as follows:

$C_{14}H_{10}O_2 + H_2$	Benzoyl hydride (bitter almond oil)
$C_{14}H_{10}O_2 + O + H_2O$	Benzoic acid
$C_{14}H_{10}O_2 + Cl_2$	Benzoyl chloride

[1] *Jahresb.*, 1828, 8, 292.

[2] *Jahresb.*, 1833, 13, 192.

$C_{14}H_{10}O_2 + Br_2$	Benzoyl bromide
$C_{14}H_{10}O_2 + I_2$	Benzoyl iodide
$C_{14}H_{10}O_2 + N_2H_4$	Benzamide
$C_{14}H_{10}O_2 + C_2N_2$	Benzoyl cyanide
$C_{14}H_{10}O_2 + S$	Benzoyl sulphide
$C_{14}H_{10}O_2 + O + C_4H_{10}O$	Benzoic ether

This was not, however, the first example of a compound radical. In 1815 Gay-Lussac, in controlling Bertholet's experiments on the composition of hydrocyanic acid, obtained cyanogen by heating mercuric cyanide, and by the action of the halogens on hydrocyanic acid prepared the chloride, bromide, and iodide of cyanogen. This example of a compound radical, as well as that of sulphocyanogen and ammonium, were overlooked, partly because they were ranked with inorganic substances, partly because Lavoisier's original conception of a radical necessarily implied that part of a substance of which the other part was oxygen. It should be observed that in benzoyl we have a modification of Lavoisier's definition of a compound radical inasmuch as benzoyl contained oxygen.

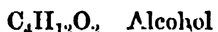
Liebig and Wöhler's discovery was soon followed by that of other radicals. The radicals of salicylic and cinnamic acids were shown, the former by Piria, and the latter by Dumas and Peligot, to form each a series of derivatives similar to that of benzoic acid, and were termed respectively *salicyl* and *cinnamyl*. Ten years later the theory of the compound radical received further confirmation in a brilliant research of Bunsen upon *cacodyl*.

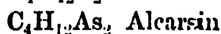
In 1760 Cadet obtained by the distillation of potassium acetate with oxide of arsenic a fuming and fetid liquid, which inflamed spontaneously in the air and was extremely poisonous. It was called 'Cadet's fuming liquid'. These uninviting properties deterred chemists for seventy years from satisfying any curiosity they might have conceived as to its composition, and they contented themselves with stating its properties and method of preparation.

Dumas was the first to analyse it, and gave it the formula $C_8H_{12}As_2$; but Bunsen soon afterwards ascertained that the liquid prepared by the above method contained oxygen and had the formula $C_4H_{12}As_2O$, which he called *cacodyl oxide* (κακώδης, stinking).[1] From this he obtained, by means of the halogen acids, cacodyl chloride, bromide, iodide, and also the cyanide, fluoride, sulphide, selenide, cacodylic acid, and, finally, by the action of metallic zinc on the chloride, the

[1] Pogg., *Ann.*, 1837, 40, 219; 1837, 42, 145; *Annalen*, 1841, 37, 1; 1842, 42, 14; 1843, 46, 1; Ostwald's *Klassiker*, No. 27.

radical cacodyl itself $C_4H_{12}As_2$, which he also named *alcarsin* (alcohol-arsenic) to indicate its relation to alcohol.


$C_4H_{12}O_2$ Alcohol


$C_4H_{12}As_2$ Alcarsin

He termed cacodyl a true organic element possessing the character of a metal. This analogy is readily understood if we write Kd for the cacodyl radical and compare it with a metal such as calcium.

Cacodyl	$C_4H_{12}As_2$	Kd	Ca
Cacodyl oxide	$C_4H_{12}As_2O$	KdO	CaO
Cacodyl chloride	$C_4H_{12}As_2Cl_2$	$KdCl_2$	$CaCl_2$
Cacodyl cyanide	$C_4H_{12}As_2Cy_2$	$KdCy_2$	$CaCy_2$
Cacodyl sulphide	$C_4H_{12}As_2S$	KdS	CaS

Liebig's Definition of a Compound Radical. Although this research was the product of a later period, Liebig's original definition of a compound radical has undergone no change.[1] He says, speaking of cyanogen, 'we call this a radical because (1) it is the invariable constituent of a series of compounds, (2) it can be replaced by other simple bodies, and (3) in its combinations with a simple body the latter may be substituted by equivalents of other simple bodies. Of these three conditions, two must be fulfilled.' These conditions made it essential that in a series of simple reactions the radical or group of elements should be shown to remain intact, and not only to be capable of combining with elements to form compounds, but also of being replaced by them.

It is evident from this statement that the author conceived the elements of which the radical was composed to be united by a bond which joined them together more firmly than the other elements in the compound. The particular group composing the radical upon which the choice fell was a matter of much diversity of opinion. This is specially noteworthy in the case of ether and alcohol and their derivatives.

The Radical 'Ethyl'. We have already referred to the etherin theory of Dumas and Boullay and the comparison which they drew between olefiant gas and ammonia. There existed at the time another view of the constitution of ammonia and its salts. The theory that ammonium played the part of a metallic radical in its salts was suggested by Davy, and afterwards supported by Ampère and Berzelius. It appealed to the dualists, for it enabled them to establish an analogy between the composition of the salts of ammonia

[1] *Annalen*, 1838, 25, 2.

and those of the alkali metals This view was now revived by Liebig, and, in place of etherin C_4H_8 and its analogue ammonia NH_3, the new radical C_4H_{10}, termed by Liebig etheryl or ethyl[1] (αἰθήρ, ether, and ὕλη, substance), took its place beside ammonium.

$C_4H_{10}Cl_2$	Hydrochloric ether.	$N_2H_8Cl_2$	Ammonium chloride.
$C_4H_{10}O$	Ether.	N_2H_8O	Ammonium oxide (present in the salts).
$C_4H_{10}O + H_2O$	Alcohol.	$N_2H_8O + H_2O$	Ammonium hydrate.
$C_4H_{10}O + N_2O_5$	Nitric ether.	$N_2H_8O + N_2O_5$	Ammonium nitrate.
$C_4H_{10}O + C_4H_6O_3$	Acetic ether.	$N_2H_8O + C_4H_6O_3$	Ammonium acetate.

Berzelius who had, as we have seen, abandoned the etherin theory, accepted the new doctrine, for its basis was dualistic, inasmuch as ether appeared as an oxide. He and Liebig, however, held different views on the constitution of alcohol. Liebig regarded it, from its relation to ether, as the hydrate of ether, whereas Berzelius considered it to be the oxide of a different radical, C_2H_6.[2] One reason advanced by Berzelius was the difference in properties between sulphovinic acid obtained by the action of sulphuric acid on alcohol, and isethionic acid, prepared by Magnus by the action of sulphuric acid (SO_3) on alcohol and ether.[3]

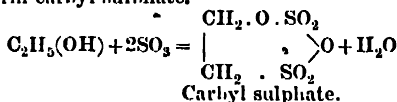
The two substances are isomeric and saturate the same amount of base, but the barium salt of sulphovinic acid contains an atom more water than that of isethionic acid, and they are in other respects totally distinct substances. 'It is clear, therefore,' writes Berzelius in the *Jahresbericht* for 1833, 'that this atom of water cannot be present as water of crystallization, but must be there in another form, and this other form can be nothing else than a form of ether. It naturally follows that alcohol and ether are not hydrates of the same base, although they may be so regarded.'

The two formulae of the barium salts would therefore appear as $2C_2H_6O + 2SO_3 + BaO$ for the sulphovinate, and $C_4H_{10}O + 2SO_3 + BaO$ for the isethionate.[4]

[1] *Annalen*, 1834, 9, 1. [2] *Jahresb.*, 1833, 13, 194.

[3] *Annalen*, 1833, 6, 163; Pogg., *Ann.*, 1833, 27, 367.

[4] According to modern views the formation of isethionic acid from ethionic acid and carbyl sulphate would be represented as follows: alcohol and sulphur trioxide unite to form carbyl sulphate.



Carbyl sulphate.

Carbyl sulphate is decomposed by water, first into ethionic, and finally into isethionic acid:



Ethionic acid. Isethionic acid.

But there were additional reasons. Berzelius contended that the dissimilarity in properties of alcohol and ether could not be attributed to the presence or absence of water. Nor was it probable that in alcohol the water could have so strong an affinity for the ether (with which in the free state it cannot be induced to combine) that a dehydrating agent, like barium oxide, can produce from alcohol no trace of ether.

Growth of Organic Chemistry, 1830–1840. Whilst the various disputants were urging the claims of rival radicals, their activity in the laboratory was not suspended. Organic chemistry was steadily advancing and widening its boundaries by new discoveries, which followed one another in rapid succession. The foundation of the great edifice of aromatic chemistry was being laid, upon which the next generation was to build new and important industries. Mitscherlich had obtained *benzene* from benzoic acid by distillation with lime, identical with Faraday's hydrocarbon from oil gas, and formed *nitrobenzene*, *benzenesulphonic acid*, *chlorobenzene* and certain other derivatives. Runge had found *kyanol*, afterwards identified as aniline, and *carbolic acid* in coal-tar. Liebig had obtained *chloral* and *chloroform* by the action of chlorine on alcohol, and had determined the composition of *acetone*, *aldehyde*, and *acetal*. Dumas and Peligot had isolated *methyl alcohol* in the pure state from wood spirit, and Dumas and Cahours had prepared *amyl alcohol* from fusel oil. In both cases a number of derivatives had been obtained offering a close analogy with those from ordinary alcohol. Zeise had discovered the *mercaptans*, and Regnault had studied the action of potash on Dutch liquid, and obtained the compound we now call *vinyl chloride*. The formula of the new compound was written $C_4H_6Cl_2$ and, according to Regnault, contained the radical C_4H_6, which he termed *aldehydène*, subsequently changed to *acetyl*. In the meantime a partial reconciliation had been arrived at between Liebig and Dumas, when the latter was won over to the 'radical' views of Liebig, and the result was a joint article which appeared in 1837, and of which the following is an abstract.[1]

'Organic chemistry possesses its own elements, which sometimes play the part of chlorine or oxygen (e.g. cyanogen), and sometimes that of a metal (e.g. ethyl, benzoyl, cacodyl). Cyanogen, amide, benzoyl, the radicals of ammonia, of the fats, of alcohol and its derivatives, are the true elements of organic nature, whereas the

[1] *J. prakt. Chem.*, 1837, 14, 298; *Compt. rend.*, 1837, 5, 567.

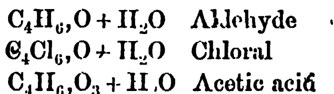
simplest constituents, carbon, hydrogen, oxygen, and nitrogen, only reappear when the organic matter is completely destroyed.'

The truce did not last long and when the new radical, acetyl, appeared, Liebig seized upon it in order to explain the constitution of those compounds, which, like Zeise's platinum compounds and Dumas' oxamethane, contained no ethyl radical, without having recourse to the etherin theory to which he was a firm opponent. Like his predecessors he established an analogy with ammonia and its derivatives by introducing into the latter the radical *amide*.[1]

Letting Ac stand for acetyl, C_4H_6, and Ad for amide, N_2H_4, the series of compounds appeared with the following formulae:

AcH_2	Olefiant gas.	AdH_2	Ammonia.
AcH_4	Ethyl.	AdH_4	Ammonium.
AcH_4O	Ether.	AdH_4O	Ammonium oxide.
AcH_4Cl_2	Ethyl chloride.	AdH_4Cl_2	Salammoniac.
AcH_4O+H_2O	Alcohol.	—	—
AcH_4S+H_2S	Mercaptan.	AdH_4S+H_2S	Ammonium sulphide.
AcH_2+2SO_3[2]	Isethionic acid.	AdH_2+SO_3	Rose's anhydrous ammonium sulphate.
—	—	$2Ad+2CO$	Urea.
—	—	$Ad+2CO$	Oxamide.
AcH_4, $Ad+2C_2O_3$	Oxamethane.	—	—

The new theory also enabled Liebig to include in his scheme aldehyde, chloral, and acetic acid, which appeared as follows:



$C_4H_6,O+H_2O$ Aldehyde
$C_4Cl_6,O+H_2O$ Chloral
C_4H_6,O_3+H_2O Acetic acid

The introduction of the new acetyl radical C_4H_6 into alcohol and its derivatives never actually replaced the older ethyl radical which continued to be used by the German chemists, whilst etherin was retained in France.

The Chemistry of Compound Radicals. With the year 1840 the first chapter in the history of organic chemistry may be said to close. Although organic chemistry was still concerned with products of a vital force, and with the compounds derived from them by the action of chemical reagents, the dominant idea was the compound radical. It was around the compound radicals that the various organic substances were grouped. In Liebig's treatise, which was published

[1] *Annalen*, 1839, 30, 129.

[2] This formula represents the anhydride of the acid. After Regnault's discovery of its preparation from sulphur trioxide and olefiant gas, it was usually represented as a compound of etherin and sulphuric anhydride

in 1840, all the well-defined compound radicals, whether containing carbon or not, are included. Separate chapters are devoted to amide, oxide of carbon (the radical of oxalic acid), cyanogen, benzoyl, cinnamyl, salicyl, ethyl, acetyl, methyl, formyl, cetyl, amyl, and glyceryl. They were hypothetical groups which might or might not be capable of separation, but their admission was a necessity and their existence in the compound more than probable. Organic chemistry was defined by Liebig as the *chemistry of the compound radical*.

Theory of Substitution. Meanwhile a movement had begun, which, gathering force as it advanced, swept away two ruling principles, the one, the electro-chemical theory, the other, the pre-existence, as it was termed, of radicals as unalterable groups of elements, or proximate constituents of organic compounds. It was the direct result of the study of a chemical process which has been termed *substitution*. The idea of substitution was not a new one. The substitution of a metallic oxide for water in an acid hydrate to form a salt, and Mitscherlich's discovery that the crystalline form of a compound is often retained when one element replaces another, were well known to chemists. Among organic compounds, the action of chlorine on hydrocyanic acid had been found by Gay-Lussac to give cyanogen chloride, Liebig and Wöhler had obtained benzoyl chloride from bitter almond oil, and Faraday prepared carbon sesquichloride, C_2Cl_6, from Dutch liquid in the same manner.

Dumas' Law of Substitutions. In 1834 Dumas' attention had been directed to the action of chlorine on organic compounds by observing, as Gay-Lussac had previously done, that when wax is bleached by chlorine a portion of the hydrogen is replaced by chlorine. He found also that, when chlorine acts upon turpentine, for every volume of hydrogen removed an equal volume of chlorine enters. He then repeated Liebig's experiments on the action of chlorine and bleaching powder upon alcohol, and carefully analysed the products. From the result of these researches he formulated, in 1834, the following *empiric law of substitutions*.[1]

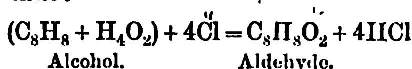
1. If a body containing hydrogen be acted upon by chlorine, bromine, or iodine, or oxygen, for every atom of hydrogen which it loses, it takes up one atom of chlorine, bromine, or iodine, or half an atom of oxygen.

2. If the compound, besides hydrogen, contains oxygen, the same rule holds without modification.

[1] *Ann. Chim. Phys.*, 1834, 56, 113.

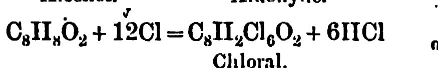
3. If a body contains water in addition it first loses the hydrogen of the water without replacement; if hydrogen is then removed, it is replaced in the above manner.

The first two propositions require no comment; the third was introduced in order to explain such reactions as the conversion of alcohol into chloral, and alcohol into acetic acid. The reactions were written thus:



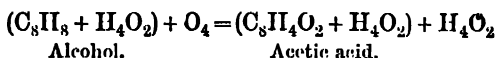
$$(C_8H_8 + H_4O_2) + 4Cl = C_8H_8O_2 + 4HCl$$

Alcohol. Aldehyde.



$$C_8H_8O_2 + 12Cl = C_8H_2Cl_6O_2 + 6HCl$$

Chloral.



$$(C_8H_8 + H_4O_2) + O_4 = (C_8H_4O_2 + H_4O_2) + H_4O_2$$

Alcohol. Acetic acid.

The study of substitution, to which Dumas gave the name of *metalepsy* (*μετάληψις*, exchange), attracted many of the French chemists, among whom were Peligot, Malaguti, and Regnault, who studied the action of chlorine on ethyl chloride and ether, and Laurent, who investigated its action on naphthalene,[1] and with Regnault, on Dutch liquid. As a result of Laurent's observations, the following rules were added to the laws of Dumas:

'When chlorine, bromine, oxygen, or nitric acid replace hydrogen in a hydrocarbon, the hydrochloric acid, hydrobromic acid, nitrous acid or water formed are either liberated or remain combined with the product'.[2]

Laurent's Nucleus Theory. Upon this foundation Laurent constructed, in 1837, his nucleus theory.[3] Laurent assumed that every organic compound contained a hydrocarbon nucleus or radical. These were the *primary nuclei* (noyaux fondamentaux), and were so chosen that the elements composing them were present in even numbers (see p. 28). Other elements or groups of elements can be added on to the primary nuclei. When the hydrogen in the primary nucleus was replaced by equivalents of other elements, the halogens, oxygen, nitrogen, &c., *secondary nuclei* (noyaux dérivés) were produced, and the compound remained intact. It was only when the elements of the nucleus were permanently removed that complete decomposition of the substance ensued. The primary nucleus was compared to a prism, the solid angles of which corresponded to carbon, and the edges to hydrogen. If these edges are replaced by others the geometrical form is unchanged, but should they be

[1] *Ann. Chim. Phys.*, 1835, 59, 196. [2] *Ann. Chim. Phys.*, 1836, 60, 223.
[3] *Ann. Chim. Phys.*, 1837, 61, 125; see also Gmelin's *Handbook*, 7, 18, 30.

removed, the system falls to pieces. To the central prism other geometrical figures can be attached, on removing which the original form reappears. The following examples may serve to illustrate the theory. By the alternate action of chlorine and potash on olefiant gas, a number of chlorinated compounds had been obtained. These were supposed to contain the primary nucleus C_4H_8. The compounds were written as follows, the nomenclature being that of Dumas and Peligot:

Ethérène	C_4H_8
Etherène hydrochlorate (hydrochloric ether)	$C_4H_8 + H_2Cl_2$
Chloréthérase (Regnault's acetyl chloride)	$C_4H_6Cl_2$
,, hydrochlorate (Dutch liquid)	$C_4H_6Cl_2 + H_2Cl_2$
Chloréthérose	$C_4H_4Cl_4$
,, hydrochlorate	$C_4H_4Cl_4 + H_2Cl_2$
Chloréthérise	$C_4H_2Cl_6$
,, hydrochlorate	$C_4H_2Cl_6 + H_2Cl_2$
Chloréthérose	C_4Cl_8
Chloride étherosique (Faraday's sesquichloride of carbon)	$C_4Cl_8 + Cl_4$

A similar series was derived from methylene and naphthalene, whilst alcohol and its oxidation products appeared as follows:

Alcohol	$C_4H_8 + H_4O_2$
Aldehyde	$C_4H_6O + H_2O$
Acetic acid	$C_4H_6O + O_2$

Although Laurent's formulae bore a certain resemblance to those of the etherin theory, they really embodied an important new principle, namely, that when chlorine and bromine replace their equivalent of hydrogen, the former *take the place* of the latter, and play to some extent the same part in the new compound, in consequence of which the compound retains a certain similarity to the parent substance.

The theory amounted to a revolution. We cannot wonder that it should have served as a direct challenge to Berzelius and the followers of the electro-chemical school. The principle, once admitted, that chlorine, an electro-negative element, could take the place of hydrogen, an electro-positive element, and do so without changing the typical properties of the new compound, was to shake the very foundation of dualism; for we must remember that it was this opposite negative and positive character which served to link the atomic units in a compound; it was this dual conception which saw a new hydrocarbon radical in every compound in which hydrogen was replaced by another element.

Berzelius was not slow in replying. His first contemptuous comment on the new formulae of Laurent appeared in his *Jahresbericht* for 1837: 'I consider it superfluous to enlarge further on such a theory.' He then directed his attack against Dumas, who at once repudiated the revolutionary views of Laurent:[1] 'To represent me as saying that when chlorine replaces hydrogen it plays the part of the hydrogen, is to attribute to me an opinion against which I strongly protest, as it is opposed to everything I have written on this subject. The substitution theory expresses only the relation which exists between the hydrogen which disappears and the chlorine which takes its place,' and further on, 'It is an empiric rule which is of value so long as it holds; if any one has given it an extension which was not in my mind, I am not responsible.' When, however, Dumas afterwards (1839) obtained trichloracetic acid by passing chlorine into acetic acid, and found that the new compound not only retained the characteristic acid property of the original substance, saturating the same amount of base and forming salts and esters, but yielded chloroform with potash, as acetic acid yielded marsh gas, the analogy between the two was complete, and Dumas henceforth participated in Laurent's views.

'It is clear,' wrote Dumas, 'that if I accept this doctrine, which is based upon facts, I cannot attach any weight to an electro-chemical theory which has been the dominant idea upon which Berzelius has sought to construct a universal system.'

'But these electro-chemical ideas, this special polarity which is assigned to the atoms of simple bodies, do they rest upon such clear facts that they may rank as articles of faith? Or, if they are considered as hypotheses, have they the property of adapting themselves to the facts with such certainty that they can be utilized in chemical investigations? It must be conceded that such is not the case.'

'Isomorphism—a theory based upon facts—has been a true guide in mineral chemistry, and, as is well known, has little in common with electro-chemical theories.'

'Now, in organic chemistry, the theory of substitution plays the same part as isomorphism in inorganic chemistry, and indeed it may happen that future experience will show that both views are related and spring from the same cause, which may be combined in a common expression.'

'For the present, from the conversion of acetic into chloracetic acid and from that of aldehyde into chloral, from the fact that the

[1] *Compt. rend.*, 1838, 6, 699.

whole of the hydrogen is replaced by chlorine, volume for volume, without changing their original nature we must conclude:

'*That there exist in organic chemistry certain types which remain as such even after their hydrogen has been replaced by an equal volume of chlorine, bromine, or iodine.*'

'That is to say, the theory of substitution rests on facts, and on the most striking facts, of organic chemistry.'

Dumas' Theory of Types. Dumas' *Theory of Types* incorporated his former law of substitutions and Laurent's propositions under a somewhat modified form.[1]

The new theory was introduced in order to emphasize the difference between the substituted compound and the parent substance in which the general character or type was preserved, as in the case of acetic and chloracetic acid or aldehyde and choral, on the one hand, and, on the other, those substitution products (more especially where oxygen replaced hydrogen) which were not related by similarity of properties as exemplified by alcohol and acetic acid or marsh gas and formic acid. The former belonged to the same *chemical* type and the latter to a *mechanical* or *molecular* type.

The two groups may be illustrated by the following examples, using Dumas' notation:

Chemical type.		*Mechanical type.*	
Acetic acid	$C_4H_2H_6O_4$	Alcohol	$C_4H_6H_6O_2$
Chloracetic acid	$C_4H_2Cl_6O_4$	Acetic acid	$C_4H_6H_2O_4$
Aldehyde	$C_4H_2H_6O_2$	Marsh gas	$C_2H_2H_6$
Chloral	$C_4H_2Cl_6O_2$	Formic acid	$C_2H_2O_3$

Dumas pointed out that the properties of a compound lay in the arrangement of its atoms and not in their nature. He wrote: 'Lavoisier's compounds were a combination of a combustible element with a combustion supporting element. The electro-chemical theory saw in these an electro-negative and an electro-positive element, which is a modification of the same thing. This dualism is unnecessary to explain the constitution of chemical compounds, the parts of which may be compared to those of a planetary system which are held together by mutual attraction. They may be more or less numerous, simple or complex. In the constitution of the compound they play the same part as the simple elements, Mars or Venus, in our planetary system, the atomic group Earth with its moon, or Jupiter with its satellites. If in such a system one part is replaced by another of a different kind, equilibrium is maintained, and, if the replaced and

[1] *Ann. Chim. Phys.*, 1840, (2), 73, 73.

replacing elements resemble one another, the new compound has similar chemical properties to the original one. If, however, they differ they belong to a mechanical system, and the chemical similarity is difficult to recognize.'

There was a tendency to carry this theory of substitution too far, and when Dumas suggested that even carbon might undergo substitution[1] the idea was ridiculed by Liebig.[2]

In the meantime Liebig had himself contributed to the overthrow of the electro-chemical theory.

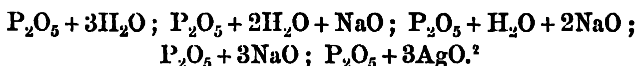
The Constitution of Organic Acids. Liebig published in 1838[3] a paper 'On the Constitution of Organic Acids'.

The organic acids, it must be remembered, were the only class of substances which had representatives of a strictly analogous character among inorganic compounds, and any new theories respecting the structure of the latter would necessarily include organic acids. Before discussing the subject of Liebig's paper, it may be well to gain some idea of the views generally held in regard to the constitution of acids and salts. In inorganic chemistry, salts of oxyacids were assumed to be compounds of non-metallic oxides (called acids) with metallic oxides or bases. What we now term acid was the hydrate, the water being sometimes termed basic water, which indicated that in the formation of salts it was replaceable by a base. The same principle was applied to organic acids and salts, C_2O_3 standing for oxalic acid and $C_4H_6O_3$ for acetic acid, as already pointed out (p. 7). The molecular weight of an acid was derived from the neutral salts, which were assumed to contain one equivalent of base united to one of acid. Thus, sulphuric acid and the sulphates were written $SO_3 + H_2O$, $SO_3 + KO$, $SO_3 + AgO$, $SO_3 + CaO$, &c. An acid salt was a neutral salt combined with an equivalent of hydrated acid; a basic salt was a neutral salt with an additional equivalent of base. Bisulphate of potash, as it was then called, had the formula $SO_3 . H_2O + SO_3 . KO$. The molecular weight of an organic acid, like citric acid, was determined from its silver or lead salt. According to Berzelius $C_4H_4O_4 + AgO$ was the silver salt of citric acid, $C_4H_4O_4 + H_2O$ was the acid hydrate, and $C_4H_4O_4$ stood for the acid.[4] The varying basicity of acids was not recognized.

There was one exception to the above rules. In ordinary sodium phosphate the ratio of one equivalent of base to one of acid would

[1] *J. prakt. Chem.*, 20, 281. [2] *Annalen*, 1840, 33, 308.
[3] *Annalen*, 1838, 26, 113; Ostwald's *Klassiker*, No. 26.
[4] These formulae are obviously incorrect. The correct formula of the acid hydrate determined by the method described would be $C_4H_4O_4 + H_2O_{\frac{1}{3}}$.

give the formula (leaving out water) $PO_{2\frac{1}{2}} + NaO$, and this was therefore altered to $P_2O_5 + 2NaO$. The additional molecule of water, which we now recognize as forming a part of the compound, was included in the total water of crystallization. But a curious anomaly was discovered by Clark. In attempting to prepare anhydrous sodium phosphate he found that the ordinary crystalline phosphate loses water on heating, but forms a new salt, which has properties entirely distinct from common sodium phosphate, and does not unite at once with water to form the original compound.[1] The explanation was given by Graham. He showed that there exists in phosphoric acid three molecules of water, which are replaceable by one, two, or three molecules of base as follows:



$$P_2O_5 + 3H_2O\,;\; P_2O_5 + 2H_2O + NaO\,;\; P_2O_5 + H_2O + 2NaO\,;$$
$$P_2O_5 + 3NaO\,;\; P_2O_5 + 3AgO.^{[2]}$$

He distinguished between the three molecules of combined water and the water of crystallization. When the water of crystallization is expelled no change in chemical properties results; but if the temperature is raised so as to drive off the combined water, then salts of new acids are formed. He prepared in this way the sodium salts of pyro- and meta-phosphoric acids and the acids themselves by heating ordinary phosphoric acid. Graham proved in this way that, whereas ordinary phosphoric acid has three replaceable atoms of water and is therefore tribasic, pyrophosphoric acid contains two and is dibasic, and metaphosphoric acid only one, and is therefore monobasic.

Liebig carried these researches into the field of organic chemistry. He found, for example, that citric acid, like phosphoric acid, formed three series of salts, and that the analysis of the acid dried at 100° did not agree with the formula of Berzelius, but must be represented by $C_{12}H_{10}O_{11} + 3H_2O$. The analogy between phosphoric and citric acid could be carried even further, for citric acid on heating loses water and is converted into pyrocitric acid (citraconic acid), which is dibasic. The old rule for determining the molecular weight of an acid as the quantity, which saturates one equivalent of base, had to be relinquished, and it now became necessary to fix beforehand the basicity of the acid before the weight of the molecule could be ascertained. Liebig's rule was to find, in the first instance, whether the acid was capable of uniting with more than one kind of base. Thus tartaric acid was dibasic, as it formed, in the case of Rochelle salt

[1] *Phil. Trans.*, 1833, 2, 284.

[2] The equivalent notation in which phosphorus had double its present combining weight represented phosphoric acid as PO_5.

and tartar emetic, a tartrate of potash and soda, and of potash and antimony oxide. Sulphuric acid, on the other hand, remained monobasic, because a sulphate with two bases was unknown. The acid sulphates continued to be written as a double molecule of acid and neutral salt.

At the close of the paper Liebig reviews the whole question of the presence of water in acids. He saw that the separation of water by the action of a base on an acid is an insufficient explanation, for the oxygen of the water may be conceived as coming from the metallic oxide just as well as existing already combined in the acid hydrate. Moreover, in the case of organic acids the presence of water is improbable, since the anhydrous acids are purely fictitious entities, having never been isolated.

Liebig revived the theory of Davy (1809) and Dulong (1819) in regarding acids as compounds of hydrogen,[1] and he pointed out, as they had done, that it was illogical to separate the halogen acids, hydrocyanic acid, and hydrogen sulphide from the oxyacids by an artificial barrier. He further contended that if, for example, silver sulphocyanide is $Cy_2S + SAg$, the silver, being already present as sulphide, should not separate in this form when hydrogen sulphide acts upon the salt, but the reverse actually happens; if, then, silver sulphocyanide is $Cy_2S_2 + Ag$ and the sulphocyanic acid is $Cy_2S_2 + H_2$, then cyanic acid must be $Cy_2O_2 + H_2$, and so on with the other acids.

The conception of acids as compounds of hydrogen did not at once replace the older view, but by affording a simple and legitimate interpretation of the formation of salts from acids by the substitution of hydrogen by a metal, it threw doubt on the validity of the electro-chemical theory.

Gerhardt and Laurent. The theory of polybasic acids was subsequently modified and expanded by Charles Gerhardt and Auguste Laurent, two chemists whose names will always be linked together in the history of chemical science. They were essentially reformers, and, like many ardent reformers, they relentlessly threw over time-honoured formulas and rode rough-shod over cherished traditions. In their place they set up empiric rules of classification and artificial systems of notation and nomenclature which were

[1] Davy supported his view on the ground that potassium chlorate parts with its oxygen on heating and forms potassium chloride, and concluded that this stronger affinity of the metal for the acid than for oxygen must also obtain among the oxyacids. Dulong based his opinion on the constitution of the oxalates, which he regarded as carbon dioxide united to the metal, thus: $2CO_2 + Pb$ and oxalic acid $2CO_2 + H_2$.

difficult to understand or assimilate. They thus alienated the sympathy of their fellow chemists, who treated them in a manner now painful to contemplate. Although no action on the part of Gerhardt and Laurent justified such treatment, yet it must be confessed that had they adopted a less uncompromising attitude towards men who were their seniors in years and reputation, it would have gone far to soften the asperities of a situation which they unfortunately helped to create.[1]

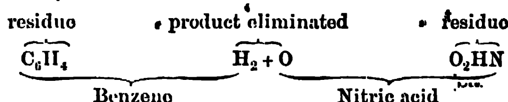
The Unitary System. Gerhardt and Laurent clearly saw the confusion into which the electro-chemical theory had plunged organic chemistry, and they set themselves resolutely to extricate it from the network of vague and unprofitable speculations in which it had become involved. In Laurent's preface to his *Chemical Method*[2] he writes: 'The confusion which reigns in the ideas is even greater than that which obtains in the facts; for the principles upon which the majority of chemists rely for the explanation and co-ordination of facts are so vague, so uncertain, that not only do two chemists explain the same phenomena in two different ways, but even one and the same person abandons an explanation he gave yesterday for a new one he proposes to-day, and which he will abandon to-morrow for a third.' Gerhardt, in his *Précis de Chimie Organique* (1844), says much the same thing: 'When a chemist at the present time observes a reaction or analyses a new substance his first care is to conceive a little theory which shall explain the phenomena according to electro-chemical principles, and it is customary to create a hypothetical radical in order to adapt these principles to the new compound'; and again, 'Six or seven formulae have been suggested for alcohol, each observer trying to support his own; but after all, each of these formulae is but the expression of one or two reactions. Upon one thing only are we agreed, and that is the empiric formula for alcohol.' They laid aside the electro-chemical theory and the doctrine of the compound radical as fixed, proximate constituents. Organic compounds were no longer binary compounds, nor an arrangement of certain fixed groups of elements. They were, as Dumas expressed it, *édifices simples*, simple structures, in which one or more elements might be replaced by others. In opposition to the binary or dualistic principle the system was termed *unitary*. Reactions were expressed by equations, but not in the customary fashion, for they did not, by introducing radicals, formulate any preconceived internal structure of

[1] *Vie de Charles Gerhardt*, by Grimaux and Gerhardt, Masson & Cie, Paris, 1900.
[2] *Chemical Method*, by A. Laurent, trans. by W. Odling, Cavendish Society's Publications, London, 1855.

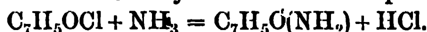
the substances taking part, but merely indicated the interchange of constituents. The interchange was ascribed to the stability of such combinations as water, hydrochloric acid, carbonic acid, and ammonia, which, though they might be eliminated in the process, did not therefore pre-exist in any of the reacting substances. The new compound was formed by a double decomposition accompanied by the removal of a part of the reagent, in combination with part of the reacting substance, and the residues or *restants* then united.

Gerhardt's Theory of Residues. This embodied the principle of Gerhardt's system of residues and copulated compounds which appeared in 1839.[1] The fundamental idea was that of substitution, for, according to Gerhardt's rule, 'the element which is removed is replaced by the equivalent of another element or by the residue of the reacting substance.'

Gerhardt represented the action of nitric acid on benzene thus:



The residue HNO_2 replaced the atoms of hydrogen in benzene. The action of ammonia on benzoyl chloride was expressed in a similar way:



$$C_7H_5OCl + NH_3 = C_7H_5O(NH_2) + HCl.$$

Chlorine is removed from benzoyl chloride and hydrogen from ammonia, and the two residues unite to form benzamide.

Conjugated Compounds. The introduction of the term *copula* or *conjunct* arose in the following way: the action of nitric acid on benzene, or sulphuric acid on alcohol has no parallel in that of an acid on a base in inorganic chemistry, except that water is removed. Nitrobenzene is not a salt, for the acid and base cannot be replaced by other acids or bases, and in sulphovinic acid and the sulphonic acids the sulphuric acid can no longer be detected by ordinary reagents. The original constituents are completely masked and the residues may have their atoms differently arranged. They are, as Dumas expressed it, in a *form of substitution*.[2] The action of nitric acid on benzene can be represented as a substitution, as already pointed out, but not that of sulphuric acid on a hydrocarbon or alcohol, for the saturation capacity of the acid, according to the formulae then in use, remains unchanged. Different bases may

[1] *Ann. Chim. Phys.*, 1839, 72, 180.

[2] This *form of substitution* bears a close resemblance to non-ionisable compounds.

saturate the acid, but the organic constituent remains permanently attached. This indifferent residue which was attached to the acid was called by Gerhardt[1] the copula and gave rise to the term *copulated compounds* (sels copulés), which, however, very soon lost its original meaning. When the different basicities of the acids was recognized, and sulphuric acid became in Gerhardt's system dibasic then the term copulated compound or *conjugated compound*, as it was called by Dumas, received the following interpretation:[2] 'The basicity or saturation capacity of a conjugated compound is always less by one unit than the sum of the basicities belonging to the two original substances.' Thus benzenesulphonic acid, obtained from benzene and sulphuric acid, is monobasic, whilst benzenesulphobenzoic acid, which is formed from benzoic acid and sulphuric acid, making a total of three units of basicity, is dibasic. When the majority of organic compounds with acids was embraced by the term conjugated, this rule was applied to determine the basicities of acids. It was taken as a proof that nitric acid was monobasic because it formed a neutral compound with benzene.

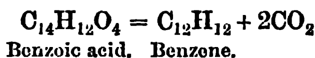
Formulae of Gerhardt and Laurent. The attempt to attach to the terms atom, molecule, volume, and equivalent a definite and logical meaning and to establish a rational system of chemical formulae was one of the most important services rendered by Gerhardt and Laurent to chemical science. It has already been stated that the different opinions which existed on the interpretation and in the application of these expressions, was such that many chemists had renounced the atomic system of Berzelius and taken refuge in Gmelin's equivalent notation. Their troubles were not at an end and difficulties still pursued them. It could scarcely be otherwise so long as the molecule remained an indefinite quantity.

Gerhardt[3] introduced a new principle. Reviving Avogadro's law, though in a somewhat restricted sense, he proposed to make the equivalents, by which he implied molecules, of all volatile compounds and gases correspond to equal volumes. For this reason he reinstated Berzelius' old formula H_2O for water, seeing that it was composed of two volumes of hydrogen and one of oxygen. From the density of mercury vapour, mercuric oxide received the formula Hg_2O in place of HgO, and the other basic oxides were referred to the same general type M_2O. The result was that the atomic weights of all

[1] *Ann. Chim. Phys.*, 1839, 72, 186; Gmelin's *Handbook*, 7, 213.
[2] *Précis de Chimie Organique*, I, 98; Laurent's *Chemical Method*, p 211.
[3] *Précis de Chimie Organique*, I, 52.

the metals were halved, whereby only the alkali metals and silver received their present values.

Law of Even Numbers. In his original memoir published in 1842 Gerhardt[1] determined the molecular weight by taking the weight of four volumes of vapour (compared with one of hydrogen). Finding that by so doing the number of molecules of water or carbonic acid removed in a chemical decomposition was always even, he proposed to double the molecular weights of these substances whereby they would become equivalent to ammonia N_2H_6 and correspond to four volumes. The decomposition of benzoic acid into benzene or of lactic acid into lactide were usually represented as follows:



$$C_{14}H_{12}O_4 = C_{12}H_{12} + 2CO_2$$

Benzoic acid. Benzene.



$$C_6H_{12}O_6 = C_6H_8O_4 + 2H_2O$$

Lactic acid. Lactide.

It naturally followed that every organic compound contained an even number of carbon atoms, which suggested to Gerhardt and Laurent the idea embodied in their empiric 'law of even numbers', according to which the sum of the carbon and oxygen atoms on the one hand and of hydrogen, the halogens metal and nitrogen, on the other, was divisible by 2.

These views were very soon modified. In the *Précis de Chimie Organique* already referred to, in place of four volumes the two volume basis of molecular weights is adopted, and all the formulae are halved. Hydrochloric acid, ammonia and water appear as HCl, NH_3 and H_2O, ether is $C_4H_{10}O$ and alcohol C_2H_6O, &c. The Law of Even Numbers was restricted to the sum of the hydrogen halogens, nitrogen, phosphorus and arsenic atoms. The law still holds, and depends on the quadrivalency of carbon. Though at the time purely empirical, it had the effect of drawing attention to many formulae, which proved to be inaccurate and which were corrected and simplified.

Basicity of Acids. The halving of the atomic weights of the metals and the introduction of the two volume standard of molecular weights, brought out clearly the relation between related compounds. Acetic acid was now written $C_2H_4O_2$ and silver acetate $C_2H_3AgO_2$, oxalic acid was $C_2H_2O_4$ and silver oxalate $C_2Ag_2O_4$. The basicity of the acid appeared as the number of hydrogen atoms replaceable by

[1] *Revue scientifique de Quesneville*, 1872.

a metal, and *basic water* necessarily vanished. The series were written as follows:

Monobasic.		*Dibasic.*		*Tribasic.*	
Nitric acid	$NO_3.H$	Sulphuric acid	$SO_4.H_2$	Phosphoric acid	$PO_4.H_3$
Formic "	$CHO_2.H$	Oxalic "	$C_2O_4.H_2$	Citric "	$C_6H_5O_7.H_3$
Acetic "	$C_2H_3O_2.H$				

Other criteria of basicity were afterwards added by Gerhardt and Laurent. It was no longer essential that an acid to be dibasic should form a double salt with two different bases, as defined by Liebig (p. 23). An acid, if monobasic, formed one salt, one ether and one neutral amide. It was dibasic if it formed an acid and neutral salt, an acid and neutral ether and an acid and neutral amide, as well as an acid chloride containing two atoms of chlorine.

Sulphuric acid and oxalic acid were consequently dibasic and formed the following series of derivatives:[1]

Oxalic acid	$C_2O_4.H_2$	Sulphuric acid	$SO_4.H_2$
Potassium ethyl oxalate	$C_2O_4(C_2H_5)K$	Potassium sulphate	$SO_4.K_2$
Diethyl oxalate	$C_2O_4(C_2H_5)_2$	Potassium bisulphate	$SO_4.KH$
Oxamide	$C_2O_2(NH_2)_2$	Sulphovinic acid	$SO_4(C_2H_5)H$
Oxamic acid	$C_2O_3(NH_2)H$	Ethylic sulphate	$SO_4(C_2H_5)$

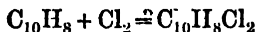
The radicals, at first entirely discarded by Gerhardt, were afterwards introduced into his residues. It was clear that in a substance like acetic ether some kind of fixity existed between the constituent parts, acetic acid and alcohol, from which it was obtained and into which it could easily be converted.

Gerhardt's System of Classification. We cannot conclude an account of Gerhardt's contributions to organic chemistry without a brief reference to his system of classification which appeared in the *Précis* of 1844. He begins by defining organic chemistry as *the chemistry of carbon compounds*, and proceeds to show how living nature has elaborated the most complex of these substances, the simpler ones being products of their decomposition. The latter may be obtained artificially; but the chemist has not yet succeeded in building up the former. He then proceeds to explain how a simple classification may be obtained by arranging compounds having similar properties according to the number of carbon atoms which they contain, and which he termed *échelle de combustion*. In the different series the carbon and hydrogen appear in the ratio of one to two. Expanding an idea which Dumas had applied to the organic acids, and Schiel (1842) to the alcohols, Gerhardt pointed out that if *R* stands for this ratio, then marsh gas and the paraffin series are

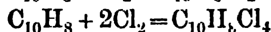
[1] Laurent's *Chemical Method* (Eng. trans.), 61, 76, and 225.

represented by R^{+2}, the alcohols by $R^{+2}O$, and the acids by RO^2, &c. To these series he gave the name of *corps homologues*. He arranged all organic compounds according to the number of their carbon atoms on the same rung of his 'ladder', and called it a *family*.

Laurent's Atoms, Molecules, and Equivalents. In his new system Gerhardt regarded as synonymous the terms atom, equivalent, and volume, by which he understood what we now express by the word *molecule*. Laurent[1] drew clearer distinctions between them. An equivalent, he stated, was a number which in addition to indicating the combining weight also expressed a function of an element. Thus, the quantity of different bases required to neutralize the same quantity of acid is its equivalent. The quantity of oxygen which replaces hydrogen in a compound is its equivalent, but this does not imply an equal number of atoms; for it is generally found that an atom of oxygen will replace two atoms of hydrogen. These equivalents are not easy to determine; for different groups of elements have frequently entirely different functions, which cannot be directly compared. Manganese in the manganous salts is equivalent to calcium; in the manganates it is equivalent to sulphur (as in the sulphates); and in the permanganates to chlorine (as in the perchlorates). But if, he said, we assume that equal volumes contain an equal number of atoms (molecules), the atoms become strictly comparable quantities independent of the function of the elements they contain. In reactions with chlorine Laurent observed that the atoms taking part are invariably an even number. Thus, from naphthalene and chlorine new products are formed both by addition and substitution:



$$C_{10}H_8 + Cl_2 = C_{10}H_8Cl_2$$



$$C_{10}H_8 + 2Cl_2 = C_{10}H_8Cl_4$$



$$C_{10}H_8 + Cl_2 = C_{10}H_7Cl + HCl, \&c.$$

Adopting the suggestion made by Ampère that the atoms of hydrogen and chlorine are divisible,[2] he concluded that the elementary gases are composed of two atoms, and he then formulated the distinction between atoms and molecules, which had been pointed out so clearly forty years before by Avogadro and Ampère, and which we still accept. When atoms of hydrogen and chlorine unite they do not simply become attached; but the molecules of hydrogen and chlorine first divide into atoms:



$$HH + ClCl = HCl + HCl$$

It was then no longer necessary to distinguish, as Gerhardt had

[1] *Chemical Method*, p. 7. [2] *Chemical Method*, p. 65.

done, between the atoms of elementary gases, which were determined from the weight of single volumes, and those of volatile compounds, which were fixed by the ratio of two volumes to one of hydrogen. The molecules of all gases could now be brought into line and determined on the two volume basis. It was considerations of this nature, as well as the law of even numbers, which suggested to Laurent the formula Cy_2 for free cyanogen, instead of Cy, and $(CH_3)_2$ for that of the newly discovered radical methyl in place of CH_3.

In spite of views thus clearly expressed and fully endorsed by both Laurent and Gerhardt, it is curious to find in Gerhardt's treatise on Organic Chemistry, the first volume of which appeared in 1853, the reappearance of the atomic weights and barred symbols of Berzelius, an account of the new system being relegated to the last volume of the book. The strong prejudice which still existed in favour of the old notation is evident from Gerhardt's reply to Pobal who questioned him on the subject: 'My book would never have found a purchaser.'[1] The new system made few converts until after the appearance of the celebrated brochure of Cannizzaro in 1858,[2] in which the principle of determining molecular weights by means of the vapour density was systematically laid down and logically carried through. Until that time the equivalent notation of Gmelin became almost universal.

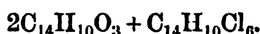
We must interrupt the narrative at this point in order to follow the fortunes of Berzelius and his followers, who still adhered to the *radical theory*, as it was termed, in opposition to the *theory of substitution.*

The School of Berzelius. After a masterly criticism of Dumas' theory of types,[3] Berzelius drifted entirely away from the French school, which now claimed Liebig and a growing number of the younger German chemists among its adherents. Nothing could shake his faith in the electro-chemical theory to which he clung more firmly than ever.

Reviving Lavoisier's definition of a radical, Berzelius wrote: 'An oxide cannot be a radical. The very meaning of the word indicates that it is the body which is united to oxygen. To regard a radical as an oxide would be equivalent to supposing that sulphurous acid (SO_2) is the radical of sulphuric acid, and manganese peroxide (MnO_2) that of manganic acid.'

[1] Ostwald's *Klassiker*, No. 30, p. 56, footnote.
[2] *Nuovo Cimento*, 1858, vol. vii.
[3] *Jahresb.*, 1840, 20, 260.

As only carbon, hydrogen and nitrogen could form part of an electro-positive radical, chlorine as well as oxygen had to disappear from the radical. Benzoyl $C_{14}H_{10}O_2$ the radical of benzoic acid, originally accepted by Berzelius, was now replaced by 'picramyl' $C_{14}H_{10}$, and the chlorine substitution products were explained as chlorides of hydrocarbon radicals. A difficulty was presented by bodies which contained both chlorine and oxygen. In such cases it became necessary to double and sometimes to treble the original formula. This led to the introduction of the copula or conjunct (*Paarling*), an expression borrowed from Gerhardt, but employed in an entirely different sense. Thus, phosgene was written $CO_2 + C_2Cl_4$, that is a compound of oxide of carbon united to the conjunct, chloride of carbon. For the same reason benzoyl chloride became:



$$2C_{14}H_{10}O_3 + C_{14}H_{10}Cl_6.$$

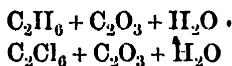
Thus Berzelius continued laboriously to construct his electro-chemical formulae upon a foundation which every moment became more insecure.[1]

Chloracetic acid and acetic acid were at first regarded by Berzelius as distinct and unrelated, acetic acid being the trioxide of acetyl C_4H_6, whereas chloracetic acid was oxalic acid united to the conjunct, chloride of carbon,



$$C_2Cl_6 + C_2O_3 + H_2O.$$

The complete analogy shown to exist between the properties of the two substances (p. 20) and Melsens' discovery (1842), that chloracetic acid can be converted by reduction with potassium amalgam and water into acetic acid, removed this shadowy distinction, and both substances now appeared as conjugated compounds of oxalic acid, one containing the radical methyl C_2H_6, and the other chloride of carbon C_2Cl_6:



$$C_2H_6 + C_2O_3 + H_2O$$
$$C_2Cl_6 + C_2O_3 + H_2O$$

The replacement of hydrogen by chlorine in the conjunct did not, according to Berzelius, materially affect the properties of the compound.

Still the one compound was virtually, although not admittedly, a substitution product of the other. In his satisfaction in the conjunct he had sacrificed the integrity of the radical and tacitly accepted the principle of substitution.

In 1845, Hofmann announced the discovery of the chlorinated

[1] *Jahresb.*, 1839, 19, 375.

and brominated anilines,[1] and later the iodo-, cyano- and nitro-anilines, which still retained the basic character of the original compound, although the property was weakened in proportion to the amount of hydrogen replaced. Berzelius explained the change by representing aniline, as he represented the alkaloids, as ammonia conjugated with a hydrocarbon $C_{12}H_8 + N_2H_6$; chloraniline would then be ammonia attached to the conjunct $C_{12}H_6Cl_2$. This view was at first accepted by Hofmann,[2] but he soon found a difficulty in explaining the anomalous behaviour of aniline oxalate, written $N_2H_6(C_{12}H_8)H_2C_2O_4$, which, unlike ammonium oxalate, refused to yield a cyanogen derivative on heating. This anomaly is removed if aniline is an amido compound; for if water is eliminated from $(C_{12}H_{10})H_4N_2 . H_2C_2O_4$ the radical phenyl $C_{12}H_{10}$ must be destroyed.[3] Thus aniline and its derivatives took rank as phenyl substitution products of ammonia.

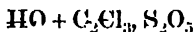
In spite of the rapidly accumulating evidence in favour of the substitution theory, Berzelius never relinquished the electro-chemical theory which he had so carefully constructed and so warmly defended.

In the *Treatise* of 1827 he prophetically wrote: 'An opinion long held often brings conviction of its truth. It hides from us its weaker points, and thereby renders us incapable of accepting adverse views.'[4] Yet nothing could be more unjust than to infer that the views of Berzelius, misleading as they proved, were unproductive.

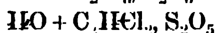
The Researches of Frankland and Kolbe. Two disciples of his school, Frankland and Kolbe, contributed between the years 1840 and 1850 a series of researches of supreme importance to organic chemistry, which now rank among the classics of chemical literature. Kolbe's opinions were influenced by the results of his first important investigation (1844) on the action of moist chlorine on carbon bisulphide;[5] for it is here that the galvanic battery is first mentioned 'as perhaps affording the experimenter a powerful instrument for disclosing the chemical constitution of organic compounds'. The reaction in question gave rise to a product, which was decomposed by potash, forming trichloromethylhyposulphuric acid (trichloromethylsulphonic acid). By the successive replacement of chlorine

[1] *Chem. Soc. Memoirs*, 1845, 2, 266; *Annalen*, 1845, 53, 1; 54, 23.
[2] *Annalen*, 1848, 67, 172.
[3] Armstrong, *Memorial Lecture*, *Chem. Soc. J.*, 1893, 655.
[4] *Treatise* (1827), vol. iii, p. 50.
[5] *Annalen*, 1845, 54, 145.

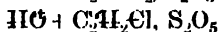
by hydrogen Kolbe obtained a series of compounds which in the barred notation of Berzelius appeared as follows:



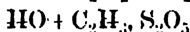
$$HO + C_2Cl_3, S_2O_5$$



$$HO + C_2HCl_2, S_2O_5$$



$$HO + C_2H_2Cl, S_2O_5$$



$$HO + C_2H_3, S_2O_5$$

The compounds were represented by hyposulphuric acid conjugated with methyl or substituted methyl radicals, forming a parallel series with acetic and chloracetic acids:



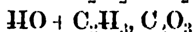
$$HO + C_2Cl_3, C_2O_3$$



$$HO + C_2HCl_2, C_2O_3$$



$$HO + C_2H_2Cl, C_2O_3$$



$$HO + C_2H_3, C_2O_3$$

'The following facts,' he concludes, 'stand in a certain relation to the new theory of substitution, and appear at first sight to lend it powerful support.'[1]

Whilst formally admitting the principle of substitution,[2] Kolbe maintained an unshaken faith in the radicals as proximate constituents of organic compounds, which, however, can undergo substitution by chlorine, bromine, amidogen, nitrogen peroxide, &c., and the object of many of his polemical writings was to rehabilitate the radical theory when the rival type theory of Gerhardt, to which reference will shortly be made, threatened to replace it.

It was in the attempt to isolate the radicals that Kolbe and Frankland discovered the first general synthetic methods for preparing the paraffins. As far back as 1834 Liebig had suggested the possibility of isolating the radicals, and even suggested a method for doing so.[3] In 1839 Löwig announced the separation of ethyl C_4H_5 by the action of potassium on ethyl chloride,[4] but it is improbable that the substance he describes was the compound in question. By acting upon ethyl cyanide with potassium Frankland and Kolbe hoped to remove the cyanogen and liberate ethyl.[5] A gas was evolved which corresponded in composition to the radical methyl C_2H_3.[6] In the expectation of preparing methyl chloride they treated the gas with chlorine, and obtained a compound which could be liquefied under pressure, and had the composition C_4H_5Cl. The substance was in fact ethyl chloride, and the hydrocarbon, from

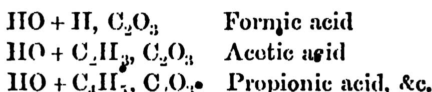
[1] *Annalen*, 1845, 54, 187.
[2] *Annalen*, 1850, 75, 211.
[3] *Annalen*, 1834, 9, 15.
[4] *Pogg., Ann.*, 1839, 45, 346.
[5] *Annalen*, 1848, 65, 269.
[6] This was explained by supposing ethyl C_4H_5 to break up into methyl C_2H_3 and olefiant gas C_2H_2.

which it was obtained, ethane; but, by some alleged discrepancy in properties, the true nature of the reaction escaped them, and the chloride was described as a conjugated compound of methyl with chloromethyl $C_2H_3 . C_2H_2Cl$.

Other hydrocarbons, and the first of the highly interesting class of organo-metallic compounds, were afterwards obtained by Frankland,[1] who, in continuation of the same line of investigation, substituted the iodides of the radicals for the cyanides and zinc for potassium. By the action of zinc on ethyl iodide a hydrocarbon was obtained, which was looked upon as the free radical, written now without barred atoms, C_4H_5,[2] whilst zinc, ethyl iodide and water, when heated under pressure, gave a hydrocarbon which was identical with that previously obtained by Frankland and Kolbe from ethyl cyanide and potassium, and was consequently methyl C_2H_3. Then followed the discovery of zinc methyl, zinc ethyl, &c., and the corresponding tin and mercury compounds and their oxides, whilst Löwig and Schweizer[3] succeeded in obtaining the antimony derivatives, Wanklyn[4] discovered potassium and sodium ethyl, and Friedel and Crafts,[5] silicon ethyl.

Not the least important of the contributions made by Kolbe and Frankland to organic chemistry, was the discovery of the synthesis of organic acids from the cyanides of the radicals.[6] This research was again suggested by Berzelius' views on the constitution of acetic acid, which represented it as oxalic acid conjugated with methyl.

It was well known that cyanogen in aqueous solution gradually changed to the ammonium salt of oxalic acid and that hydrocyanic acid could be converted by alkalis into formic acid, which was written as oxalic acid conjugated with hydrogen H, $C_2O_3 + HO$. It naturally followed that methyl cyanide should yield methyl oxalic acid, i. e. acetic acid, and so with the other cyanides. The experimental results fully corroborated these conclusions. Moreover, it brought out clearly the relationship of the acids as a series of hydrocarbon radicals having a group C_2O_3, HO in common, which translated into our present notation corresponds to carboxyl:



$HO + H, C_2O_3$	Formic acid
$HO + C_2H_3, C_2O_3$	Acetic acid
$HO + C_4H_5, C_2O_3$	Propionic acid, &c.

[1] *Quart. J. Chem. Soc.*, 1849, 2, 263; *Annalen*, 1849, 71, 171.

[2] Although Kolbe used the barred atoms in his formulae, and continued to do so as late as 1850, they were dropped by the majority of chemists, who employed only the equivalent notation (C = 6; O = 8, &c.). To avoid confusion the barred atom is henceforth omitted in all the formulae.

[3] *Annalen*, 1850, 75, 315.

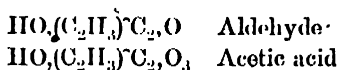
[4] *Annalen*, 1858, 108, 67.

[5] *Annalen*, 1863, 127, 31.

[6] *Annalen*, 1848, 65, 288.

In direct relation to this research stands Kolbe's investigation into the behaviour of the fatty acids on electrolysis, which resulted in the discovery of a new synthesis of the paraffins.[1] It arose out of an attempt to oxidize the oxalic acid of the acids to carbon dioxide in the hope of liberating the radical with which it was united; or in his own words, 'Starting from the hypothesis that acetic acid is a conjugated compound of oxalic acid and the conjunct methyl, I considered it, under these circumstances, not at all improbable that electrolysis might effect a separation of its conjugated constituents, and that in consequence of a simultaneous decomposition of water, carbonic acid as a product of the oxidation of oxalic acid might appear at the positive, while methyl, in combination with hydrogen, viz. as marsh gas, would be observed at the negative pole.' Although the process did not take place quite in the manner anticipated, the success of the experiments is too well known to be recapitulated in detail. The radical methyl C_2H_3 (in reality ethane) was supposed to be liberated from acetic acid, and valyl C_8H_9 (in reality octane) from valeric acid.[2] The idea of the copula or conjunct which was requisitioned by Berzelius to divide or duplicate his formulae for dualistic purposes, received from Kolbe a rather more definite signification than Berzelius had attached to it, and led to very interesting developments.

If all the organic acids are conjugated oxalic acids, it follows that the character of the radical will undergo a change in conformity with this view. For example, the original acetyl radical C_4H_6 of Regnault which was employed to show the relationship between aldehyde, acetic acid and allied compounds (p. 16), was now broken up by Kolbe into the conjunct methyl, which was attached to carbon thus, $(C_2H_3)^\frown C_2$. The radical contained two pairs of carbon equivalents, and different functions were ascribed to each. It was the pair lying outside the radical which was supposed to afford the point of attachment for oxygen and chlorine. Some of Kolbe's formulae appear as follows:[3]



$HO,(C_2H_3)^\frown C_2,O$ Aldehyde

$HO,(C_2H_3)^\frown C_2,O_3$ Acetic acid

[1] *Quart. J. Chem. Soc.*, 1850, **2**, 157; *Alembic Club Reprints*, No. 15; *Annalen*, 1849, **69**, 257.

[2] It is a curious fact that the formulae of both hydrocarbons (in Kolbe's notation they stood for C_2H_6, C_8H_{18}) are given correctly, though transposed into the modern form they would stand for CH_3 and C_4H_9. The correspondence is accidental, and arises on the one hand from the use of the double molecular formula for the acid, and on the other from the fact that the radicals unite in pairs and form substances having molecular weights double of those recognized by the author of the memoir.

[3] See footnote 2 on previous page.

$(C_2H_3)^\frown C_2, Cl_3$	Dichloro-hydrochloric ether (trichlorethane)
$(C_4H_5)O . (C_2Cl_3)^\frown C_2, O_3$	Trichloracetic ether
$(C_2H_3)^\frown C_2 \begin{cases} O_2 \\ NH_2 \end{cases}$	Acetamide
$(C_2H_3)^\frown C_2N$	Methyl cyanide

In this way methyl was recognized as an integral part not only of acetic acid, but of marsh gas $(C_2H_3)H$, which it yielded on distillation with lime, and of cacodyl oxide, written $(C_2H_3)_2As,O$, which it formed on heating the potassium salt with arsenious oxide. It explained, moreover, why the last equivalent of hydrogen in chloral $HO, (C_2Cl_3)C_2,O$ was not replaced by chlorine. The same system was applied to other acids, benzoic acid and its derivatives being represented by oxalic acid conjugated with the radical phenyl $C_{12}H_5$:

$HO,(C_{12}H_5)^\frown C_2,O_3$	Benzoic acid
$HO,(C_{12}\begin{cases} H_4 \\ NO_4 \end{cases})^\frown C_2,O_3$	Nitrobenzoic acid
$HO,(C_{12}\begin{cases} H_4 \\ NH_2 \end{cases})^\frown C_2,O_3$	Amidobenzoic acid

For the same reason that marsh gas became the hydride of methyl, benzene appeared as the hydride of phenyl $(C_{12}H_5)H$, and phenol as its oxyhydrate $HO . (C_{12}H_5)O$.[1] In this way Kolbe sought to rehabilitate the compound radical:

The constitution attached to cacodyl oxide was later extended to cacodyl and the organo-metallic compounds generally in which the radicals appeared as the conjuncts of the metals. Kolbe was, indeed, the first to interpret correctly the constitution of cacodyl to the extent of regarding it as arsenide of methyl $(C_2H_3)_2^\frown As$.

Frankland dissented from this view. It was generally admitted that the saturation capacity of a substance was retained in a conjugated compound. Oxalic acid has the same saturation capacity in the free state as when conjugated with the radical methyl C_2H_3 in acetic acid. This was not the case with the metal in the organo-metallic compounds. Cacodyl in cacodylic acid, which is the highest oxidation product, is only united to three atoms of oxygen instead of five as in arsenic acid, to two in antimony ethyl and to only one in tin ethyl. He preferred to represent these compounds as substitution products of the metallic oxides:

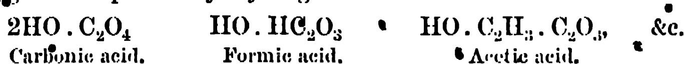
[1] *Annalen*, 1850, 76, 1.

Inorganic types.	*Organo metallic derivatives.*	
$As\left\{\begin{matrix} S \\ S \end{matrix}\right\}$	$As\left\{\begin{matrix} C_2H_3 \\ C_2H_3 \end{matrix}\right\}$	Cacodyl
$As\left\{\begin{matrix} O \\ O \\ O \end{matrix}\right\}$	$As\left\{\begin{matrix} C_2H_3 \\ C_2H_3 \\ O \end{matrix}\right\}$	Cacodyl oxide
$As\left\{\begin{matrix} O \\ O \\ O \\ O \\ O \end{matrix}\right\}$	$As\left\{\begin{matrix} C_2H_3 \\ C_2H_3 \\ O \\ O \\ O \end{matrix}\right\}$	Cacodylic acid
ZnO	$Zn(C_2H_3)$	Zincmethylium
$Zn\left\{\begin{matrix} O \\ O_x \end{matrix}\right\}$	$Zn\left\{\begin{matrix} C_2H_3 \\ O_x \end{matrix}\right\}$	Oxide of Zincmethylium
$Sb\left\{\begin{matrix} O \\ O \\ O \end{matrix}\right\}$	$Sb\left\{\begin{matrix} C_4H_5 \\ C_4H_5 \\ C_4H_5 \end{matrix}\right\}$	Stibethine
$Sb\left\{\begin{matrix} O \\ O \\ O \\ O \\ O \end{matrix}\right\}$	$Sb\left\{\begin{matrix} C_4H_5 \\ C_4H_5 \\ C_4H_5 \\ O \\ O \end{matrix}\right\}$	Binoxide of Stibethine
$Sb\left\{\begin{matrix} O \\ O \\ O \\ O \\ O \end{matrix}\right\}$	$Sb\left\{\begin{matrix} C_4H_5 \\ C_4H_5 \\ C_4H_5 \\ C_4H_5 \\ O \end{matrix}\right\}$	Oxide of Stibethylium
SnO	$Sn(C_4H_5)$	Stanethylium
$Sn\left\{\begin{matrix} O \\ O \end{matrix}\right\}$	$Sn\left\{\begin{matrix} C_4H_5 \\ O \end{matrix}\right\}$	Oxide of Stanethylium
$Hg\left\{\begin{matrix} I \\ I \end{matrix}\right\}$	$Hg\left\{\begin{matrix} C_2H_3 \\ I \end{matrix}\right\}$	Iodide of Hydrargyro methylium

It was in this memoir[1] that Frankland drew attention to the regularity subsisting between the number of the different kinds of atoms which are found in combination with the same element. This was the first announcement of the doctrine of valency or atomicity, as it was then called, which will be referred to presently (p. 50).

[1] *Phil. Trans.*, 1852, 142, 417.

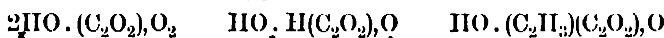
Kolbe's Views on Constitution. This relation of the organo-metallic compounds to the oxides of the metals, which Frankland first pointed out, suggested to Kolbe a further modification of his theory of conjugated compounds.[1] As cacodylic acid $HO(C_2H_3)_2AsO_3$[2] may be derived from arsenic acid $3HO.AsO_5$ by replacing two atoms of oxygen by two methyl radicals, so carbonic acid may be regarded as the mother substance of the organic acids in which part of the oxygen is replaced by hydrogen or radicals:



$2HO.C_2O_4$ (Carbonic acid.) $HO.HC_2O_3$ (Formic acid.) $HO.C_2H_3.C_2O_3$ (Acetic acid.) &c.

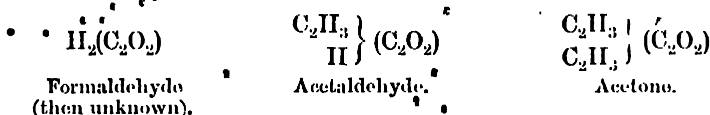
This was a counter-stroke delivered by Kolbe at the artificial inorganic types, as he regarded them, of Gerhardt's new theory which had just appeared (see p. 44). Carbonic acid, the raw material of vegetable synthesis, was on the contrary a natural type from which, as by the vital process, complex derivatives may be obtained.

In order to explain the difference of basicity between carbonic acid and the fatty acids, the group C_2O_4 in carbonic acid was split into two $(C_2O_2),O_2$, and the basicity was made to depend on the number of *extra-radical* oxygen atoms. The above formulae became



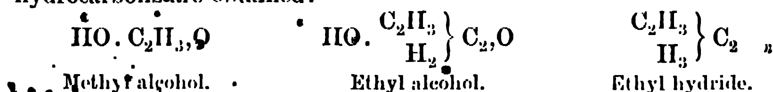
$2HO.(C_2O_2),O_2$ $HO.H(C_2O_2),O$ $HO.(C_2H_3)(C_2O_2),O$

Carbonic acid with its two extra radical oxygen atoms is dibasic, whereas formic and acetic acids, with only one, are monobasic. By replacing the last extra-radical oxygen by hydrogen or a radical the neutral aldehydes and ketones result:



$H_2(C_2O_2)$ Formaldehyde (then unknown). $\left.\begin{matrix}C_2H_3\\H\end{matrix}\right\}(C_2O_2)$ Acetaldehyde. $\left.\begin{matrix}C_2H_3\\C_2H_3\end{matrix}\right\}(C_2O_2)$ Acetone.

If in these more oxygen is substituted, the alcohols and finally the hydrocarbons are obtained:



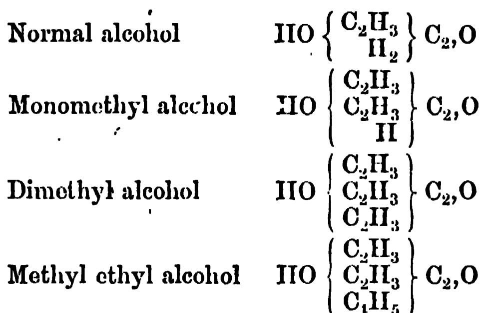
$HO.C_2H_3,O$ Methyl alcohol. $HO.\left.\begin{matrix}C_2H_3\\H_2\end{matrix}\right\}C_2,O$ Ethyl alcohol. $\left.\begin{matrix}C_2H_3\\H_3\end{matrix}\right\}C_2$ Ethyl hydride.

The curious part played by the molecules of water, which sometimes appear upon the scene and again vanish, is due to the insignificant rôle assigned to them by Berzelius and his school.

However fantastic Kolbe's formulae may now appear, the system was in so far successful that it enabled him to foretell the existence of many unknown compounds, some of which, though not all, have since been obtained. Thus, formaldehyde was predicted, and

[1] *Annalen*, 1857, 101, 257; 1860, 113, 293; Ostwald's *Klassiker*, No. 92.
[2] In these and subsequent memoirs Kolbe discarded the barred atoms.

also the secondary and tertiary alcohols. 'For,' says Kolbe, 'suppose that we introduce into the alcohols in place of one or two atoms of hydrogen the same number of methyl, ethyl, &c., atoms in the same manner (as acetone is derived from aldehyde), we shall obtain new alcohol compounds of the following constitution.'



'The monomethyl alcohol will be isomeric, not identical with propyl alcohol, and dimethyl alcohol will be isomeric with butyl alcohol.'

Two years later the first of these predictions was verified by Friedel, who isolated secondary propyl alcohol, and the second by Butlerow in 1864, who prepared tertiary butyl alcohol. They agreed in nearly every particular with the properties foretold by Kolbe.

'These compounds will probably form, with the hydracids, halogen compounds like ethyl chloride, also sulphur compounds and mercaptans, and with sulphuric acid, sulphuric ethers; but those compounds which are combined like the dimethyl alcohols will not be oxidized to aldehydes and acids, like the normal alcohols, as the two free hydrogen atoms, which in the normal alcohols are attacked, are missing. Nor can the monomethyl alcohols which still retain a free hydrogen atom be converted into acids, but by the same process of oxidation which yields aldehydes in the case of normal alcohols will convert the monomethyl alcohols into acetone.'

We must now pick up the thread of the narrative where we dropped it to follow the fortunes of the radical theory.

The standard of volumes adopted by Gerhardt and Laurent for determining molecular weights served its purpose admirably by bringing together compounds which were related to one another, but gave no information about their structure. The doctrine of residues in its original simplicity could not satisfy the aspirations of chemists in face of the powerful testimony which the researches of Frankland and Kolbe, Hofmann and many other chemists, had brought in support of the radical theory.

Williamson's Researches on Ether. It was at this critical period in the history of the science that a short and unpretentious memoir appeared, which gave an unexpected turn to the current of chemical thought. This was Williamson's research on etherification, which was first read at the meeting of the British Association at Edinburgh in 1850.[1] It is difficult to embrace in a sentence the far-reaching consequences which followed its publication. In the first place it settled the vexed question of the relation of alcohol to ether; secondly, it introduced a new and important synthetic process; it showed, further, how chemical methods might be employed in determining molecular weights; but above all it reconciled the two contending schools of thought by welding together the radical theory with Dumas' theory of types.

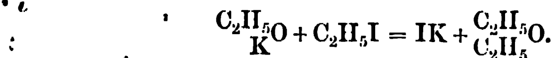
The constitution of alcohol and ether had, as we have seen, received various interpretations. Berzelius regarded them as oxides of different radicals, Liebig formulated ether as the oxide of ethyl and alcohol as its hydrate, Gerhardt in 1844 wrote their formulae C_2H_6O and $C_4H_{10}O$ from the value of their vapour densities, and Laurent in 1846 explained their relation by comparing them to potassium hydrate and potassium oxide, as the hydrate and oxide of ethyl (= Et):[2]



$$\begin{matrix} KHO & EtHO \\ KKO & EtEtO. \end{matrix}$$

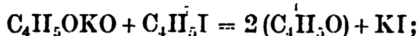
In 1850 Williamson investigated the action of ethyl iodide upon potassium ethylate in the hope of replacing the potassium by ethyl and so forming a new ethylated alcohol.

The experiment gave entirely unexpected results; for, in place of alcohol, he obtained ordinary ether. He recognized the importance of the result, explained by means of it the formation of ether, and demonstrated the correctness of his conclusions in a series of brilliant experiments. Williamson saw at once the application of Laurent's and Gerhardt's views, which he was one of the first to adopt, formulating the reaction thus:



$$\frac{C_2H_5}{K}O + C_2H_5I = IK + \frac{C_2H_5}{C_2H_5}O.$$

Kolbe strongly opposed this view and represented the reaction as follows:



$$C_4H_5OKO + C_4H_5I = 2(C_4H_5O) + KI;$$

in which, using the equivalent notation, potassium alcoholate appears as a compound of potash and ether. Substituting methyl iodide for

[1] *Quart. J. Chem. Soc.*, 1852, 4, 229; *Alembic Club Reprints*, No. 16.
[2] *Chemical Method*, p. 75.

ethyl iodide, methyl ether and ethyl ether should be formed, supposing the latter view to be correct, whilst, according to Williamson's theory, methyl ethyl ether should be formed. It was the second reaction which occurred.

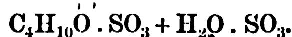
The experiments clearly demonstrated that ether is derived from alcohol by replacing one atom of hydrogen by ethyl, and consequently that it possesses a larger molecule.

It now remained to explain the formation of ether from alcohol and sulphuric acid.

The formation of ether by heating a mixture of alcohol and sulphuric acid is so simple an operation that it seems not a little remarkable that more than two centuries elapsed before the obscurity which enveloped this reaction was finally removed. As the study of this subject and the discussions which rival theories called forth engaged chemists from the very inception of organic chemistry, it will not be entirely out of place to trace the phases of its development. The first method for preparing ether is ascribed to Valerius Cordus in 1540, who called it *oleum vitrioli dulce*, the name being changed to *ether* by Frobenius in 1730. The compound was formed by heating a mixture of alcohol and strong sulphuric acid. Fourcroy and Vauquelin explained the reaction by supposing that alcohol loses a molecule of water. This agreed with the etherin theory and with Liebig's later view. The explanation was, however, open to criticism. Other dehydrating agents, like potash and baryta, effected no change of this kind, and when it was afterwards pointed out that water distilled with the ether, it was difficult to conceive how sulphuric acid could act by reason of its affinity for water if it parted with it in the process. Dabit discovered that the first action of the sulphuric acid on alcohol at the ordinary temperature was the formation of a new acid, which was not precipitated by barium salts. It was termed sulphovinic acid by Sertürner, who studied it more carefully. Then followed the discovery that the contents of the vessel after distilling off the ether could be used for the preparation of fresh quantities of the latter by adding alcohol, an observation upon which Boullay, the father of Dumas' colleague, founded the present continuous process. The first clear experimental evidence as to the nature of this curious and complex reaction is due to Hennel, an English apothecary. He proved that the formation of sulphovinic acid is essential to the process. In the first place he found by distilling equal quantities of sulphuric acid and alcohol that, as the ether distils, the quantity of free sulphuric acid increases, whilst that of the sulphovinic acid decreases. If, on the other hand, the mixture

is first diluted with water, nothing but alcohol passes over, and sulphuric acid remains in the distilling vessel. He further showed that on heating sulphovinic acid, as free as possible from alcohol or water, a certain quantity of ether distils.[1] Berzelius,[2] in his *Jahresbericht* for 1829, attributes to Hennel the view that ether is formed by the action of alcohol on sulphovinic acid, and since the latter, as Hennel first showed, is a compound of olefiant gas with sulphuric acid, ether must be a compound of olefiant gas with alcohol, a conclusion which bears a striking resemblance to the modern view; but there is nothing in Hennel's original paper which we can find in support of this statement.

Hennel rather suggests that, on heating sulphovinic acid, olefiant gas is separated in a condition which enables it to unite with one proportion of water to form ether and, when diluted, with a larger proportion of water to form alcohol. He subsequently expanded his theory as follows: When sulphuric acid and alcohol are mixed sulphovinic acid and water are formed, the latter diluting a portion of the free sulphuric acid present. On heating the sulphovinic acid, it is the water of this dilute acid which attracts the sulphuric acid of the sulphovinic acid, and enables it to split up into ether and sulphuric acid. It should be remembered that the composition of sulphovinic acid, as determined by Serullas (1829), and later by Liebig and Wöhler (1833), was represented as an acid sulphate of ether, and written



$$C_4H_{10}O \cdot SO_3 + H_2O \cdot SO_3.$$

Liebig, as the result of a series of careful experiments, showed that sulphovinic acid does not change below a temperature of 124°, but above that temperature it decomposes into ether, sulphuric acid, and sulphuric anhydride. He attempted to reconcile these facts with Hennel's views in the following manner: the alcohol on falling into the hot sulphuric acid lowers the temperature below 124° at the surface of contact, forming sulphovinic acid and water, which dilutes the sulphuric acid around it. The sulphovinic acid then diffuses into the hotter liquid where it decomposes into ether, which distils, and sulphuric anhydride which combines at once with the water of the dilute acid, regenerating concentrated acid, and is thus capable of uniting with fresh alcohol. The simultaneous distillation of water was accounted for by supposing that the ether vapour carries with it water vapour much in the same way that a high boiling volatile liquid may be distilled in steam. Mitscherlich, however, found that by passing alcohol vapour into the mixture, so that no lowering of

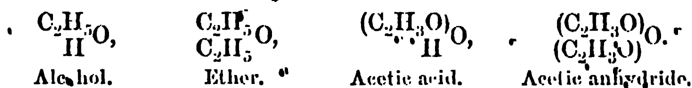
[1] *Phil. Trans.*, 1826, 2, 240. [2] *Jahresb.*, 1829, 9, 294.

temperature occurred, the formation of ether was not interrupted, and both he and Berzelius, and afterwards Graham, explained the peculiar effect of the sulphuric acid as a catalytic or contact phenomenon, by which they understood such a reaction as occurred in the presence of a substance which itself underwent no change, and for which no satisfactory explanation was forthcoming.[1]

The composition of ether being now clearly established, Williamson turned the fact to account in order to explain the production of ether from alcohol and sulphuric acid.

The explanation is the one we still adopt. The process occurs in two stages. Sulphovinic acid and water are first produced, and the sulphovinic acid reacting with a fresh quantity of alcohol forms ether and regenerates sulphuric acid. Ether and water distil whilst the sulphuric acid is free to react with fresh alcohol, and repeat the same cycle of changes. Williamson confirmed these views by showing that mixed ethers could be readily obtained by the use of two different alcohols, and prepared in this way a series of compounds containing from three to seven carbon atoms.

In reviewing his results he points out that compounds like alcohol, ether, acetic acid, and its hypothetical anhydride may be regarded as water in which one or two hydrogen atoms are replaced by the radicals ethyl and *othyl* (oxygen ethyl):



$\left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}O,$	$\left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}O,$	$\left.\begin{matrix}(C_2H_3O)\\H\end{matrix}\right\}O,$	$\left.\begin{matrix}(C_2H_3O)\\(C_2H_3O)\end{matrix}\right\}O.$
Alcohol.	Ether.	Acetic acid.	Acetic anhydride.

This memorable paper, which proved so fruitful in results and provided such a powerful stimulus to future research, concludes with the following words: 'The method here employed, of stating the rational constitution of bodies by comparison with water, seems to me to be susceptible of great extension, and I have no hesitation in saying that its introduction will be of service in simplifying our ideas, by establishing a uniform standard of comparison by which bodies may be judged of.'[2]

Gerhardt's discovery of the acid anhydrides, in the same year, by heating the acid chlorides with their sodium salts, amply justified Williamson's conclusions.

Gerhardt's New Theory of Types. In the following year, 1853, Gerhardt[3] published his new theory of types, already foreshadowed in a memoir by Chancel and himself on *The Constitution of Organic*

[1] *Jahresb.*, 1835, 15, 213. [2] *Quart. J. Chem. Soc.*, 1852, 4, 239.
[3] *Ann. Chim. Phys.*, 1853, 37, 332.

Compounds, which appeared in the *Revue Scientifique* for 1851. It was a direct outcome of Williamson's memoir on ether, though unacknowledged at the time of its publication.[1]

To understand this development we must recall a few facts. In 1849 Wurtz had obtained, by the action of potash on cyanic and cyanuric ethers, bases closely allied in smell and basic characters to ammonia, which he compared to ammonia wherein an atom of hydrogen was replaced by the radicals methyl, ethyl, and amyl.[2] Although the existence of such compounds had been foretold ten years earlier by Liebig, it was the first successful attempt to introduce radicals into ammonia. This interesting fact is recalled by Liebig himself in a note to Wurtz's paper in the *Annalen*.[3]

'If one considers the combination NH_2 or amide as a compound radical, which possesses the properties of radicals as opposed to those of acid radicals, it is clear that ammonia is the hydrogen compound of a basic radical, which is similar in composition to hydrocyanic acid, but is the reverse in properties. Hydrogen cyanide is an acid, hydrogen amide has alkaline properties, a difference due to the characters of the radicals which they contain. . . . Now we know that amide is capable of replacing equivalent for equivalent the oxygen of many organic acids, and we find that the new compounds thus produced have altogether lost the nature of acids, being indifferent in their chemical character. . . . If in the oxides of methyl and ethyl, the oxides of two basic radicals, we were able to substitute one equivalent of amide for oxygen, there cannot be the slightest doubt that we should obtain compounds perfectly similar in their behaviour to ammonia. Expressed in a formula a compound $C_4H_5 + NH_2 = E + Ad$ must have basic properties.'

The character which Wurtz attached to these compounds was soon afterwards confirmed by Hofmann, who obtained what are known as the primary, secondary, and tertiary bases by the action of the iodides of the alcohol radicals on aniline and ammonia.[4]

The organic phosphorus compounds which Paul Thénard had discovered in 1845 now received an analogous interpretation. In addition to these new classes of compounds, the acid chlorides had been prepared by Cahours[5] in 1845, and the anilides and other amides by Gerhardt and Chiozza[6] in 1853.

[1] *Vie de Gerhardt*, p. 412.
[2] *Compt. rend.*, 1848, 26, 368; 27, 241; 1849, 28, 223, 323; 29, 169, 186, 203; *Annalen*, 1849, 71, 326.
[3] *Annalen*, 1849, 71, 317.
[4] *Annalen*, 1850, 73, 91; 1851, 79, 16.
[5] *Compt. rend.*, 1845, 21, [illegible]; 1847, 25, 892.
[6] *Compt. rend.*, 1853, 37, 86.

All these groups of compounds were now referred by Gerhardt to four types. 'In expounding his theory he says: 'I do not attach to these so-called *rational* formulae, which give the molecular constitution of chemical compounds, any exaggerated value, because they are in fact only the expression of a partial truth, which in a more or less complete fashion includes a certain number of chemical changes. Such formulae, however, appear to me to have their use, for they may exert a happy influence on the development of the science, if they are viewed from the same standpoint and accord well together.'

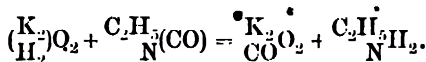
The four types which he proposes are water, H_2O, hydrogen, H_2, hydrochloric acid, HCl, and ammonia, NH_3. Each vertical series is derived from the type by replacing the hydrogen by radicals :

$\left.\begin{matrix}H\\H\end{matrix}\right\}$	$\left.\begin{matrix}H\\Cl\end{matrix}\right\}$	$\left.\begin{matrix}H\\H\end{matrix}\right\}O$	$\left.\begin{matrix}H\\H\\H\end{matrix}\right\}N$
Type.	Type.	Type.	Type.
$\left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_5\\Cl\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}O$	$\left.\begin{matrix}C_2H_5\\H\\H\end{matrix}\right\}N$
Ethyl hydride.	Ethyl chloride.	Ethyl alcohol.	Ethylamine.
$\left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_3O\\Cl\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}O$	$\left.\begin{matrix}C_2H_5\\C_2H_5\\H\end{matrix}\right\}N$
Diethyl.	Acetyl chloride.	Ethyl ether.	Diethylamine.
$\left.\begin{matrix}C_2H_3O\\H\end{matrix}\right\}$	$\left.\begin{matrix}C_7H_5O\\Cl\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_3O\\H\end{matrix}\right\}O$	$\left.\begin{matrix}C_2H_5\\C_2H_5\\C_2H_5\end{matrix}\right\}N$
Aldehyde.	Benzoyl chloride.	Acetic acid.	Triethylamine.
$\left.\begin{matrix}C_2H_3O\\CH_3\end{matrix}\right\}$	$\left.\begin{matrix}CN\\Cl\end{matrix}\right\}$	$\left.\begin{matrix}C_2H_3O\\C_2H_3O\end{matrix}\right\}O$	$\left.\begin{matrix}C_2H_3O\\H\\H\end{matrix}\right\}N$
Acetone.	Cyanogen chloride.	Acetic anhydride.	Acetamide.

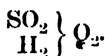
They were in a sense mechanical rather than chemical types, for the members of one type were connected together more in outward form than in properties ; but the typical formulae served admirably to express double decompositions, to indicate the relation which the function of an element bears to its position in the type, and finally, to explain cases of isomerism.

Inorganic compounds were also constructed on the system of types, nitric acid being represented by Williamson as $\left.\begin{matrix}NO_2\\H\end{matrix}\right\}O$, to which Gerhardt added Deville's nitric anhydride $\left.\begin{matrix}NO_2\\NO_2\end{matrix}\right\}O$.

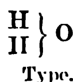
Condensed Types. In developing his views on the constitution of the ethers, Williamson had already introduced the idea of the *condensed* water type. He pointed out that it may be usefully employed in formulating the action of potash on the organic ethers.[1]

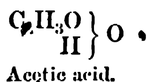


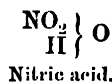
In this equation the two atoms of hydrogen in the double molecule of potash are replaced by the group CO. Williamson recognized in this the existence of what we now term a multivalent radical, which was then called by analogy with the polybasic acids, a *polybasic radical.* The group CO was therefore dibasic, or, according to Gerhardt, diatomic. The group SO_2 was regarded in the same light, the formula for sulphuric acid being derived from a condensed water type of two molecules and written

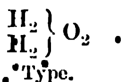


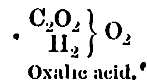
Odling extended the idea to other inorganic and organic acids, and to the metals themselves:

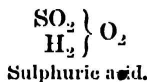

Type.

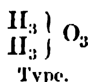

Acetic acid.

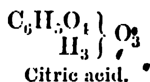

Nitric acid.

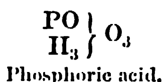

Type.


Oxalic acid.

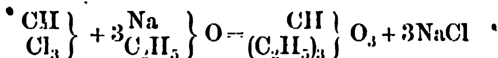

Sulphuric acid.


Type.


Citric acid.


Phosphoric acid.

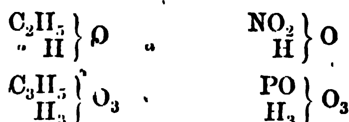
Wurtz's Researches on Glycol. In 1851 Williamson and Kay obtained orthoformic ether by the action of sodium ethylate on chloroform:[2]



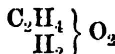
This was the first example of a tribasic hydrocarbon radical. About the same time Berthelot was engaged in the investigation of glycerine, and found that it unites in three distinct proportions with acids, forming acetins, stearins, and chlorhydrins, &c. He concluded

[1] *The Chemical Gazette*, 1851, 9, 334; *Alembic Club Reprints*, No. 16, 46.
[2] *Quart. J. Chem. Soc.*, 7, 1.
[3] *Proc. Roy. Soc.*, 1854, 7, 135.

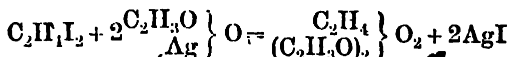
that glycerine bore the same relation to phosphoric acid that alcohol does to nitric acid:



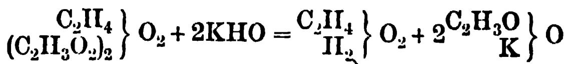
Wurtz quickly perceived that a compound intermediate between alcohol and glycerine should exist, derived from a double water type, and containing a dibasic radical. Before long he had supplied the necessary link by the discovery of glycol:[1]



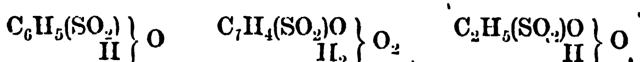
He prepared the compound from ethylene iodide and silver acetate, which, on heating together, yield ethylene acetate and silver iodide. Using the typical formulae, the equation appears thus:



Ethylene acetate on hydrolysis with potash forms glycol:



Mixed Types. The use of condensed types was shortly followed by the introduction of Kekulé's *mixed types*,[2] which he set forth in a paper *On the so-called Conjugated Compounds and the Theory of Polyatomic Radicals*. Kekulé's object was to explain the constitution of Gerhardt's new conjugated radicals, that is, the old conjugated compounds which, in their new typical garb, played the part of substituted radicals. Benzenesulphonic acid, sulphobenzoic acid, and sulphovinic acid were written



Benzenesulphonic acid. Sulphobenzoic acid. Sulphovinic acid.

Benzenesulphonic acid may be represented, according to Kekulé,[3] as derived from the two types of hydrogen and water,

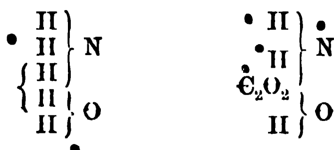


[1] *Ann. Chim. Phys.*, 1859 (3), 55, 400.

[2] *Annalen*, 1857, 104, 129.

[3] Following a suggestion of Williamson, the symbols for oxygen, carbon, sulphur were barred in Kekulé's formulae to indicate that the combining weights were double those of the equivalent notation.

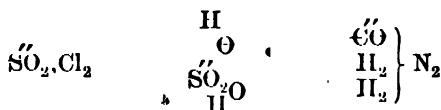
Oxamic acid may, in the same way, be referred to a mixed water and ammonia type:



Kekulé's Theory of Atomicity. Kekulé at once saw, as Williamson had previously done (p. 47), that such a fusion of types to a condensed or mixed type can only occur where a polybasic or polyatomic radical is present in the place of two or three atoms of hydrogen. Using the dashes of Odling to indicate atomicity and the double atoms, which Williamson had revived to distinguish Gerhardt's atomic weights (C = 12, O = 16) from Gmelin's equivalents (C = 6, O = 8), Kekulé defines the radicals as follows:

'A *monatomic* radical can, therefore, never hold together two molecules of the types.'

'A *diatomic* radical can unite *two* molecules of the types,' e. g.



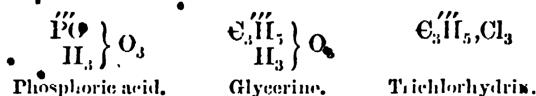
Thionyl chloride. Sulphuric acid. Urea.

or, can replace two hydrogen atoms of the type, e. g.



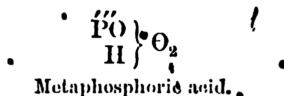
Sulphuric anhydride. Cyanic acid.

'A *triatomic* radical can unite in the same way three molecules of the types,' e. g.



Phosphoric acid. Glycerine. Trichlorhydrin.

or it can also replace three atoms of hydrogen in two molecules of water, e. g.



Metaphosphoric acid.

Perhaps the most important part of this remarkable and suggestive memoir is the reference to the basicity, i. e. valency of the individual elements.

Growth of the Theory of Valency. As the whole foundation of modern structural chemistry may be said to rest upon the theory of valency, it is necessary to trace carefully the line of thought which culminated in its development.

It is just possible that had no previous literature existed on the subject, this property of the elements would have disclosed itself to Kekulé's penetrating intellect. It is none the less true that the merit of having been the first to offer a clear exposition of the subject belongs to Frankland.

In studying the organo-metallic compounds, to which reference has been made (p. 37), Frankland was struck with the fact that there appears to be a definite saturation capacity for the metals, and that the number of radicals present affects the number of inorganic elements which attach themselves to the metal in a symmetrical fashion. It was this fact which led him to oppose Kolbe's view that the radicals are conjugated with the metal. At the close of this paper[1] Frankland expressed himself as follows: 'When the formulae of inorganic chemical compounds are considered, even a superficial observer is struck with the general symmetry of their construction; the compounds of nitrogen, phosphorus, antimony, and arsenic especially exhibit the tendency of these elements to form compounds containing three or five equivalents of other elements, and it is in these proportions that their affinities are best satisfied; thus in the ternal group we have NO_3, NH_3, NI_3, NS_3, PO_3, PH_3, PCl_3, SbO_3, SbH_3, $SbCl_3$, AsO_3, AsH_3, $AsCl_3$, &c.; and in the five-atom group NO_5, NH_4O, NH_4I, PO_5, PH_4I, &c. Without offering any hypothesis regarding the cause of this symmetrical grouping of atoms, it is sufficiently evident, from the examples just given, that such a tendency or law prevails, and that *no matter what the character of the uniting atoms may be, the combining power of the attracting element, if I may be allowed the term, is always satisfied by the same number of these atoms.*'

Two years later, in his first publication of theoretical importance, *Note on a New Series of Organic Acids containing Sulphur*,[2] Kekulé refers to the basicity of the elements. Various organic compounds of the water type such as alcohol, ether, acetic acid, and acetic anhydride were heated with the sulphides of phosphorus and the typical oxygen replaced by sulphur. He shows that the new typical formulae of Gerhardt are well adapted for expressing these changes. If, according to the equivalent notation, phosphorus chloride breaks

[1] *Phil. Trans.*, 1852, 417. [2] *Annalen*, 1854, 90, 309.

up alcohol into $C_4H_5Cl + HCl$, why should not phosphorus sulphide produce two compounds $C_4H_5S + HS$ instead of their remaining united as mercaptan? With Gerhardt's notation the change is manifest, $\left.\begin{matrix} C_2H_5 \\ H \end{matrix}\right\} O$ becomes $\left.\begin{matrix} C_2H_5 \\ H \end{matrix}\right\} S$, but with phosphorus chloride the alcohol divides up thus, $\dfrac{C_2H_5Cl}{H\ Cl}$. He writes: 'It is not merely a difference of notation, but it is an actual fact that one atom of water contains two atoms of hydrogen and only one atom of oxygen; and that for one indivisible atom of oxygen the equivalent of chlorine is divisible by two; whereas sulphur, like oxygen, is dibasic, one atom being equivalent to two of chlorine.'

In the memoir already referred to (p. 48), *On the so-called Conjugated Compounds and the Theory of Polyatomic Radicals*,[1] Kekulé's views on atomicity take a clearer and more definite shape. He says: 'The molecules of chemical compounds are formed by the union of atoms. The number of atoms of other elements which are attached to one atom of an element, or (if in the case of compound bodies one prefers not to extend the idea to elements) of a radical, is dependent on the basicity or affinity of the constituents.'

'The elements fall into three main groups:

'(1) Monobasic or monatomic, e.g. H, Cl, Br, K; (2) dibasic or diatomic, e.g. O, S; (3) tribasic or triatomic, e.g. N, P, As. From these are derived the chief types, HH, OH_2, NH_3, and the secondary types, HCl, SH_2, PH_3.' In a footnote on p. 133 he adds that carbon is tetrabasic or tetratomic.

After this defence of Gerhardt's formulae and clear exposition of atomic structure, it is curious to find Kekulé reverting to the equivalent notation in his very next memoir on the constitution of fulminating mercury; but such is the despotic power of long established custom.

In discussing the constitution of fulminating mercury, Kekulé[2] pointed out its analogy with a series of compounds which might be considered as belonging to the same type as marsh gas, using the word in Dumas' sense of one compound being related to another by substitution. He succeeded, in fact, in liberating the cyanogen as cyanogen chloride by chlorination, and converting fulminating mercury into chloropicrin.

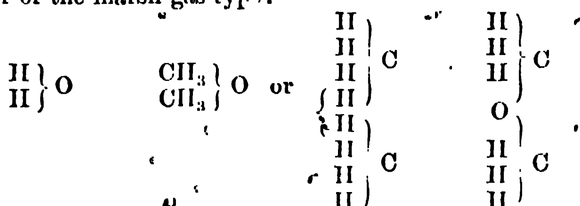
Methyl chloride, chloroform, chloropicrin, and acetonitrile were

[1] *Annalen*, 1857, 104, 133. [2] *Annalen*, 1857, 101, 200.

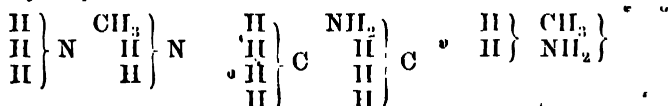
grouped with marsh gas, and written in the equivalent notation thus:

C_2	H	H	H	H	Marsh gas
C_2	H	H	H	Cl	Methyl chloride
C_2	H	Cl	Cl	Cl	Chloroform
C_2	(NO_4)	Cl	Cl	Cl	Chloropicrin
C_2	H	H	H	(C_2N)	Acetonitrile
C_2	(NO_4)	Hg	Hg	(C_2N)	Fulminating mercury

Thus Kekulé introduced a new type, that of marsh gas, and with its introduction the fixity of Gerhardt's types was dissolved; for it now became evident that the grouping of the elements depended, not on the nature of the type, but upon that of the elements themselves. As typical formulae were not intended to represent the position of the atoms, it became a matter of choice to which type a compound belonged. Thus, methyl ether may be equally well derived from the water or the marsh gas type:



Methylamine in the same way may be referred to ammonia, marsh gas, or hydrogen:



Quadrivalence of Carbon. Early in 1858 Kekulé's celebrated paper appeared in Liebig's *Annalen* on *The Constitution and Metamorphoses of Chemical Compounds, and on the Chemical Nature of Carbon*, in which are embodied his views on the valency of carbon and the linking of carbon atoms.[1] Shortly afterwards an equally remarkable memoir on the same subject by A. S. Couper[2] was published independently in the *Annales* under the title of *A new Chemical Theory.*

Kekulé's Theory. Kekulé has told, in a very graphic way, how these new ideas arose. It was during his stay in London.

'One fine summer evening I was returning by the last omnibus

[1] *Annalen*, 1858, 106, 129; Ostwald's *Klassiker*, No. 145.

[2] *Ann. Chim. Phys.*, 1858 (3), 53, 469.

"outside" as usual, through the deserted streets of the metropolis, which are at other times so full of life. I fell into a reverie, and lo! the atoms were gambolling before my eyes! Whenever, hitherto, these diminutive beings had appeared to me they had always been in motion; but up to that time I had never been able to discern the nature of their motion. Now, however, I saw how, frequently, two smaller atoms united to form a pair; how a larger one embraced two smaller ones; how still larger ones kept hold of three or even four of the smaller; whilst the whole kept whirling in a giddy dance. I saw how the larger ones formed a chain, dragging the smaller ones after them, but only at the ends of the chain. . . . This was the origin of the *Structurtheorie*."[1]

'If we consider,' writes Kekulé in his memoir, 'the simplest compounds of carbon, CH_4, CH_3Cl, CCl_4, $CHCl_3$, $COCl_2$, CO_2, CS_2, CHN, it is very striking that the amount of carbon which chemists recognize as the atom, that is, the smallest part, always unites with four atoms of a monatomic or two of a diatomic element, that generally the sum of the chemical units which are bound to an atom of carbon is equal to four. This leads to the view that carbon is tetratomic.'

'For substances which contain several atoms of carbon, one must suppose that a portion of the atoms at least is held by the attraction of the carbon, and that the carbon atoms themselves are united to one another, whereby naturally a part of the attraction of the one is neutralized by an equal attraction on the part of the other.'

'The simplest and consequently most probable case of such a union of two carbon atoms is that one unit of affinity of one carbon atom is bound to one of the other. Of these 2 × 4 units of affinity of the two carbon atoms, two will be used to unite the two carbon atoms, and six will remain over to attach the other elements. In other words the group C_2 is hexatomic. . . .'

'If more than two carbon atoms unite in the same way, the basicity of the carbon group will be increased by two units for each additional carbon atom. Thus the number of hydrogen atoms which may be combined with *n* carbon atoms is expressed by

$$n(4-2)+2 = 2n+2.$$

'. . . Up to this point we have assumed that all the atoms attaching themselves to carbon are held by the affinity of the carbon. It is equally conceivable, however, that in the case of polyatomic elements (O, N, &c.) only a part of the affinity—for example, only one of the

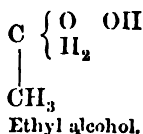
[1] *The Kekulé Memorial Lecture*, by F. R. Japp, *Trans. Chem. Soc.*, 1898, 73, 97.

two units of affinity of the oxygen, or only one of the three units of the nitrogen—is attached to carbon; so that one of the two units of affinity of the oxygen and two of the three units of affinity of the nitrogen remain over and may be united with other elements. These other elements are therefore only in indirect union with the carbon, a fact which is indicated by the typical mode of writing the formulae.'

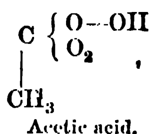
Kekulé does not recognize only this one kind of attachment of the carbons. He points out that another kind of combination may occur involving a closer union of the carbon atoms, an idea which was expanded seven years later (1865) in his theory of the benzene ring.

Couper's Theory. Couper[1] arrived at similar conclusions from a different starting-point. His paper, which is characterized by remarkable perspicuity and breadth of view, has perhaps scarcely received the full recognition which it merits. Couper begins by rejecting the type theory of Gerhardt as artificial and unphilosophical, and lays stress on the fact that the properties of compounds must in the end depend on the nature of their atoms. Gerhardt's system is like referring a language to certain types of words, from which all others are formed, instead of to the individual letters. The atoms, he considers, are held together by virtue of two properties, *elective affinity* or chemical affinity and *degree of affinity*, which corresponds exactly to our word valency.

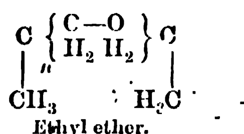
In regard to carbon (1) it unites with an even number of hydrogen atoms, and (2) it unites with itself. The maximum number of atoms with which it can combine is four. The following are some of the formulae proposed by Couper which, apart from the presence of the double atom of oxygen, bear a complete resemblance to those in modern use ($C = 12$; $O = 8$):



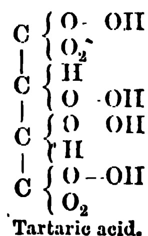
Ethyl alcohol.



Acetic acid.



Ethyl ether.

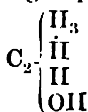


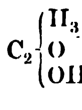
Tartaric acid.

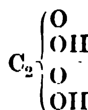
[1] *Nature*, 1909, p. 32J.

The two papers by Kekulé and Couper are the foundations upon which the modern structural formulae of organic compounds rest. It must not be supposed that the typical formulae were at once discarded in favour of the modern notation. On the contrary, the typical notation was in general use for many years after the above memoirs had appeared, and was even retained in Kekulé's textbook of organic chemistry which was published as late as 1866. It is evident, from the facts recorded in the next chapter having reference to the basicity of lactic acid, that the true significance of Kekulé's and Couper's views had not then (1863) taken root.

Modern Structural Formulae. It is in fact difficult to assign any particular date to the introduction of the modern structural notation. Its adoption was the result of a gradual and almost imperceptible development. Frankland made a distinct advance by deriving his compounds from the marsh gas or its condensed type, and breaking up the rest of the molecule attached to the typical carbon atoms into tervalent groups thus:


Alcohol.


Acetic acid.


Oxalic acid.

Although there is evidence that the principle of carbon linkages, like that suggested by Couper, was fully recognized before its actual adoption,[1] it was not until 1866 that the first appearance of the modern system of notation occurs in two papers by Erlenmeyer,[2] followed in 1867 by a clear exposition of the subject by Frankland.[3]

The necessity for the replacement of rational by structural formulae became more and more emphasized with the growth of the subject, and especially with the extension of the views on isomerism which demanded a more delicate and perfect language for its expression.

REFERENCES.

History of Chemistry, by A. Ladenburg, trans. by L. Dobbin. Clay, Edinburgh, 1905.

History of Chemistry, by E. von Meyer, trans. by G. McGowan. Macmillan, London, 1898.

Rise and Development of Organic Chemistry, by C. Schorlemmer, edited by A. Smithells. Macmillan, London, 1891.

Treatise on Chemistry, Vol. III, Pt. i, Introduction, by Roscoe and Schorlemmer. Macmillan, London, 1881.

Chemical Society Memorial Lectures, 1893-1900. Gurney & Jackson, London.

[1] Kekulé's *Lehrbuch der organ. Chem.*, vol. i, pp. 161 and 174.
[2] *Annalen*, 1866, 137, 351; 139, 211. [3] *Annalen*, 1867, 142, 1.

CHAPTER II

THE VALENCY OF CARBON

The early history of valency has been described in the introductory chapter (p. 50). Whilst its later development, especially in connection with organic chemistry, has been attended by results of the highest theoretical and practical value, the subject as a whole has made little advance. This is due to the apparently variable character of the property in every element including carbon, and is plainly indicated by the number of more or less unsatisfactory attempts to find a comprehensive generalisation.

The term valency is applied to the saturation capacity of one element for other elements, and must not be confused with the *strength* of the attachment or chemical affinity; it is in fact noteworthy that the lowest valency is found among those elements in the two end groups of the periodic system which exhibit the greatest affinity, or, as Hinrichsen[1] puts it, 'the energy content of an atom is the greater the smaller its active valency.'

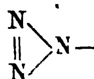
The various speculations on the relation existing between valency and affinity and the origin of the phenomena will be discussed presently.

As hydrogen is one of the elements of lowest combining capacity which rarely unites with more than one atom of a second element, it might serve as a useful standard for determining the valency of the other elements; but the small number of hydrides which it forms, especially with the metallic elements, rather restricts its application. The halogens which might be employed in place of hydrogen cannot always be relied on, as they do not possess a constant valency and form compounds such as H_2F_2, KI_3 and a whole series of oxides. Another method which might be employed is to divide the atomic weight by the equivalent of the element as determined by electrolysis

[1] *Annalen*, 1904, 366, 168.

or by the composition of the oxide. According to Faraday's law the same quantity of electricity passed through an electrolyte liberates equivalent weights of the different elements, or, in other words, equivalent weights of different elements convey the same quantity of electricity. But in this case it is found that a metal in different states of combination, such as iron in ferrous and ferric salts, exhibits different valencies, the first liberating 28 and the second 18·6 parts of iron compared with one of hydrogen. The use of the oxide presents difficulties of another kind, for the equivalent in the case of Pb_3O_4 would give a valency value for lead determined by the fraction 207/77·6.

Returning to the first method, how are we to interpret the valency of nitrogen in the two compounds, ammonia NH_3 and azoimide N_3H? Here a very simple explanation suffices. In both compounds the nitrogen is tervalent, but in the second the nitrogen atoms are linked together in the form of a univalent group:



This formulates the mutual attachment of similar multivalent atoms and introduces an entirely new conception into the idea of valency. It was a fundamental part of Kekulé's and Couper's theory of the structure of carbon compounds, and has become so interwoven with the idea of valency that its intrinsic novelty is apt to be overlooked. All-important as the conception has turned out in its application to the compounds of carbon, which stands almost alone as an element of definite valency, it has afforded the widest interpretation in determining the structure of the compounds of most of the other elements.

Thus, in the case of alumina, Al_2O_3, we may formulate a structure in which two atoms of metal or of oxygen, or the three atoms of oxygen, or, again, an alternate atom of aluminium and oxygen are directly attached, so that any arrangement may be devised to suit the desired valency of the atoms under consideration. In short, whilst the linking of atoms has afforded a firm foundation for building up the structure of compounds with elements of definite valency, its employment in other cases has generally served to increase the number of possible formulae.

Valency, a Variable Quantity. Influenced by the success which attended the application to carbon of the principle of linkages, Kekulé was led to infer that valency was a definite and unalterable quantity

bound up with each atom. The variable valency of certain elements, especially of the nitrogen and halogen groups of the periodic system, subsequently led to the complete abandonment of this view. It was impossible, for example, to reconcile the structure of NH_4Cl as consisting of NH_3 in molecular attachment to HCl with Meyer and Lecco's observation that diethylmethylamine + methyl iodide gave the same product as dimethylethylamine + ethyl iodide and also with the existence of the numerous optically active ammonium compounds (Part II, p. 304).

If, with Kolbe, we regard each element as possessing a maximum valency, a view which has been widely adopted, the question arises as to how this maximum value may be ascertained, for it is a curious fact that in the periodic table the oxygen value rises from group I to group VII, whilst the hydrogen value rises to group IV and then falls again. If we adopt the valency of the highest oxide we are confronted with the uncertain value for oxygen, which sometimes appears to function as a quadrivalent atom. On the other hand, the atomic weight being known, the periodic classification or the *atomic number* (see p. 97, footnote) affords at times a valuable guide.

Abegg and Bodländer[1] regard each atom as possessing the same total number of valencies, namely eight, which are distributed between positive and negative, the positive diminishing from 7 to 1 in the first seven groups of the periodic system and the negative increasing in the same order. Of these two kinds the positive or negative predominates in each atom and is termed the *normal* valency, whilst the subordinate kind is called a *contravalency*. In the middle or fourth group, which includes carbon, neither predominates, and this is supposed to explain the stability of carbon in its union with both electropositive and electronegative elements, as in methane and carbon tetrafluoride. The distribution of normal and contra-valencies in the seven groups is as follows:

normal	+1 +2 +3		−3 −2 −1
		±4	
contra	−7 −6 −5		+5 +6 +7

The weak point of the scheme is the existence of the seven contra-valencies among the alkali metals, for which at present there appears to be no evidence.

According to Clayton,[2] this decrease in the valency of an element for hydrogen in the more electronegative groups cannot be due to

[1] *Zeit. anorg. Chem.*, 1899, **20**, 453; 1901, **39**, 330.
[2] *Trans. Chem. Soc.*, 1916, **109**, 1046.

decrease of affinity, and must therefore have relation to some other factor which increases by a constant quantity from group to group. If this is so, the difference should be capable of being detected by reference to the actual hydroxyl derivatives of these elements or their dehydrated forms.

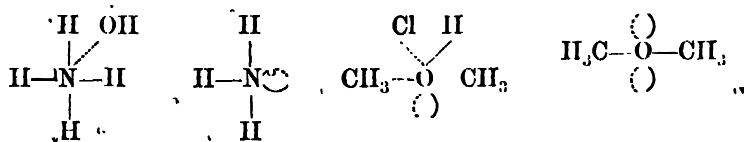
Thus, taking the series containing four hydrogen atoms having the maximum valency of their fully hydrated forms, the elements in groups V to VIII will be represented as follows:

Group.	V.	VI.	VII.	VIII.
Hydrated form	EH_4OH	$EH_4(OH)_2$	$EH_4(OH)_3$	$EH_4(OH)_4$
	$-H_2O$	$-2H_2O$	$-3H_2O$	$-4H_2O$
Dehydrated form	EH_3	EH_2	EH	No hydrid
e.g.	NH_3	OH_2	ClH	

Clayton distinguishes between the *primary* valency which reaches a maximum of 4 and a *secondary* valency which is determined by the number of hydroxyl groups. If one each of the primary and secondary valencies unite or neutralize one another, the effective valency will be lowered by two. For example, if the secondary valency in group V, which binds the hydroxyl, unites with one of the primary valencies which attaches the hydrogen, the total valency will be lowered by two and NH_3 will result. In group VI, H_2O, and in group VII, ClH will be formed, whilst the elements in group VIII do not combine with hydrogen.

Clayton indicates the primary and secondary valencies by a continuous and a dotted line respectively, which, when unattached, are represented as forming a loop.

Ammonium hydroxide and ammonia and methyl ether and its additive compound with hydrogen chloride are represented by the following formulae:

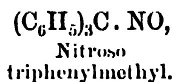


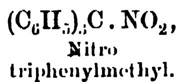
Tervalent Carbon. Although the valency of carbon has offered fewer anomalies than that of any other element in the interpretation of the structure of its numerous compounds, there exists one example, namely, triphenylmethyl $C(C_6H_5)_3$ in which there is reason to believe that carbon, at least in solution, is tervalent. There is intrinsically nothing novel or surprising in the existence of a combined atom with one unused valency, for nitrogen in nitric oxide, NO, must possess a free valency whether oxygen is bi- or quadrivalent. It may be

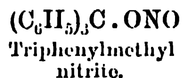
pointed out that in both compounds the unsaturated element is attached to an electronegative group or atom. Triphenylmethyl contains the strongly electronegative group $(C_6H_5)_3$ united to carbon, whereas in nitric oxide the nitrogen is linked to electronegative oxygen. Such compounds as CH_3, NH_2, or NH_4 in which the carbon and nitrogen are combined with electropositive elements are unknown. These and similar facts have led Michael[1] to draw the conclusion that union with negative atoms can produce self-saturation, but not if the combination includes positive ones. The tendency for carbon and nitrogen to polymerise (that is, for similar atoms to unite) is promoted by union with 1, 2, or 3 atoms of hydrogen. Thus CH, CH_2, and CH_3 appear, not as free entities, but as acetylene, ethylene, and ethane, and NH_2 as hydrazine.

Werner,[2] who views valency as a quantity which may be differently distributed according to the nature of the atoms or groups involved (see p. 85), considers that the phenyl groups in triphenylmethyl saturate more of the carbon affinity than, say, hydrogen atoms, leaving less affinity for further union. The compound is, in short, more saturated than methyl.

Triphenylmethyl.[3] In 1900 Gomberg,[4] in attempting to prepare hexaphenylethane $(C_6H_5)_3C \cdot C(C_6H_5)_3$ by the action of finely divided silver on triphenylmethyl chloride (bromide or iodide) in benzene solution, obtained a colourless, crystalline compound having the composition of the required hydrocarbon, but possessing very unusual properties. Though colourless in the solid form, it dissolves in most organic solvents with a distinct orange yellow colour. It is apparently unsaturated, for it combines greedily with free oxygen to form a peroxide $(C_6H_5)_3CO \cdot CO(C_6H_5)_3$, with the halogens to form triphenylmethyl halide, with hydrogen, in presence of finely divided platinum, to form triphenyl methane, with nitric oxide and nitrogen dioxide to form the nitroso compound with the first, and a mixture of nitro compound and nitrous ester with the second.[5]

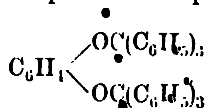

$(C_6H_5)_3C \cdot NO$,
Nitroso triphenylmethyl.


$(C_6H_5)_3C \cdot NO_2$,
Nitro triphenylmethyl.


$(C_6H_5)_3C \cdot ONO$
Triphenylmethyl nitrite.

[1] *J. prakt. Chem.*, 1899, 60, 295.
[2] *Neuere Anschauungen auf dem Gebiete der anorganischen Chemie*, p. 79.
[3] For a more detailed account of the subject the following should be consulted: Gomberg, *J. Amer. Chem. Soc.*, 1914, 36, 1144, and *Das Triphenylmethyl* by J. Schmidlin, *Chemie in Einzeldarstellung*, vol. vi, Enke, Stuttgart, 1911.
[4] *Ber.*, 1900, 33, 3150.
[5] Schlenk and Mair, *Ber.*, 1911, 44, 1169.

It also forms an additive compound with quinone,[1]



Moreover, it unites with a variety of organic solvents, paraffins, olefines, and aromatic hydrocarbons, ethers, aldehydes, ketones, esters, and nitriles, and with carbon disulphide and chloroform, in all of which two molecules of triphenylmethyl are combined with one molecule of the organic solvent in the form of well-defined crystalline substances, which are, however, easily dissociated on heating. It also enters into reactions with phenol,[2] primary and secondary amines, phenylhydrazine[3] and diazomethane.[4] Dissolved in ether out of contact with oxygen it combines with metallic sodium.[5] The sodium compound $NaC(C_6H_5)_3$ reacts normally with alkyl halides, forming alkyltriphenylmethanes, and undergoes condensation with ketones and esters very much after the manner of the Grignard reagent[6] (p. 208).

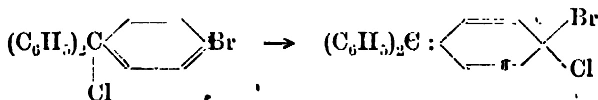
Since Gomberg first obtained triphenylmethyl, a large number of similar compounds containing a variety of aryl radicals have been prepared, and they all possess the same striking characteristics. They combine readily with free oxygen, &c., and though with few exceptions colourless in the solid state, yield a variety of coloured solutions when dissolved.[7] The difficulty encountered in determining the true structure of these substances arises from the fact that whereas some of these compounds, such as tribiphenylmethyl $(C_6H_5C_6H_4)_3C$ prepared by Schlenk and his co-workers,[8] are unimolecular in solution (determined by the cryoscopic method), others, for example, triphenylmethyl, are mainly bimolecular.[9] It would, therefore, appear that in addition to the solid, colourless compound there are two coloured substances, a bi- and unimolecular compound existing in the dissolved state. But Schmidlin has shown that in a solution of triphenylmethyl, the colourless and yellow modification exist side by side,[10] forming an equilibrium mixture which varies with the solvent and the temperature. For the freshly dissolved substance, which is at first

[1] Schmidlin, *Ber.*, 1910, 43, 1298.
[2] Schmidlin, *Ber.*, 1912, 45, 3180.
[3] Schlenk and Bornhärdt, *Ber.*, 1911, 44, 1175.
[4] Schlenk and Bornhärdt, *Annalen*, 1912, 394, 183.
[5] Schlenk and Marcus, *Ber.*, 1914, 47, 1664.
[6] Schlenk and Ochs, *Ber.*, 1916, 49, 608.
[7] Schmidlin. *Ber.*, 1912, 45, 3171, 3183.
[8] Schlenk, Weickel, and Herzenstein, *Annalen*, 1910, 372, 1; Schlenk and Renning, *Annalen*, 1912, 394, 180.
[9] Gomberg, *Ber.*, 1904, 37, 2019.
[10] *Ber.*, 1908, 41, 2471.

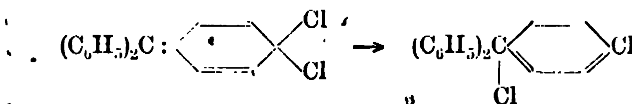
colourless, becomes quickly yellow. On shaking the solution in contact with air it loses its colour owing to the formation of the insoluble peroxide, when the yellow colour rapidly reappears as a fresh quantity of the colourless compound passes into the coloured modification. It therefore follows that the colourless and coloured compounds undergo isomeric change, but that the coloured modification is the more reactive of the two. Schmidlin has further shown that the coloured substance is in all cases unimolecular, and, though the quantity in triphenylmethyl is small, there is sufficient present (5 per cent. in benzene, 17 per cent. in naphthalene) to impart a yellow colour to the liquid.

What then is the relation between the colourless bimolecular compound and the coloured unimolecular compound?

The question has been answered by comparing the properties of triphenylmethyl and triphenylmethyl chloride. Both substances are colourless in the crystalline state, and triphenylmethyl chloride also yields colourless solutions; but both dissolve in liquid sulphur dioxide with a yellow colour, and both exhibit a fairly high conductivity. They therefore offer a close analogy. It is frequently found that isomerisation from a colourless to a coloured substance is accompanied by a change from a benzenoid to a quinoid structure, and this has been shown to occur in the case of *p*-brometriphenylmethyl chloride. Though silver chloride has no action on the substance when dissolved in benzene, in sulphur dioxide solution the bromine atom is replaced by chlorine, and on evaporating the solvent colourless *p*-chlorotriphenylmethyl chloride is obtained.[1] The change is readily explained on the assumption of an intermediate half-quinoid or *quinol* form first proposed by Kehrmann for the coloured salts of triphenylmethyl[2]

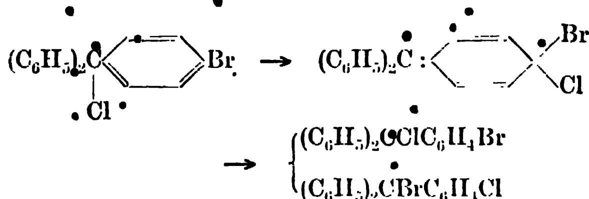


The quinoid halogens thus become labile, and an interchange of the chlorine of the silver chloride for bromine occurs, which on removal of the solvent passes into *p*-chlorotriphenylmethyl chloride.

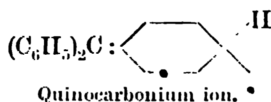


[1] Gomberg, 1909, 42, 406.
[2] *Ber.*, 1901, 34, 2815; see also, *Colour and Structure*, this volume, Part II.

Again, by simply dissolving p-bromotriphenylmethyl chloride in sulphur dioxide and removing the solvent a mixture of p-bromotriphenylchloride and p-chlorotriphenylbromide is produced:



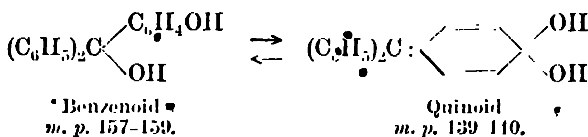
In this way triphenylmethyl chloride in isomerising to the yellow modification passes into the quinol form, and at the same time undergoes ionization into a basic ion,



Quinocarbonium ion.

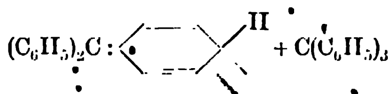
to which Gomberg has given the name quinocarbonium, and an acid ion. The coloured salts are termed quinocarbonium salts.

The existence of hydroxytriphenylcarbinol in a yellow and colourless modification, melting respectively at 139–140° and 157–159°, which are interconvertible (acids and the action of light produce the quinoid, whilst alkalis promote the benzenoid form), points to the same explanation.[1]



Benzenoid *m. p.* 157–159. Quinoid *m. p.* 139–140.

What, then, is the nature of the yellow ionized compound present in the sulphur dioxide solution of triphenylmethyl? By analogy it should consist of the basic quinocarbonium ion and an acid ion, which may be the tervalent radical,

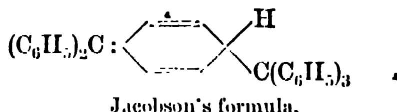


On the assumption that dilution does not change the equilibrium between two dynamic isomers, whereas ionization is known to do so,

[1] Gomberg, *J. Amer. Chem. Soc.*, 1913, 35, 1035.

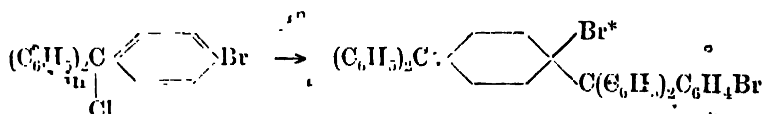
Piccard[1] determined the effect of dilution on the intensity of the colour of triphenylmethyl, and showed that it does not follow Beer's law,[2] but that the colour is intensified; in view of recent observations on the effect of solvents on the equilibria of dynamic isomers,[3] Piccard's conclusion that ionization occurs cannot be sustained. Nevertheless, the observation is of interest.

The existence of the corresponding unionized compound of the formula,

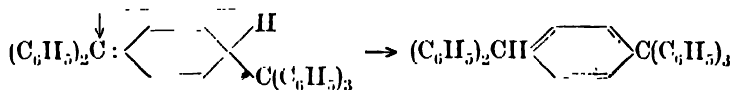


Jacobson's formula.

which was first suggested by Jacobson, is supported by observations of Gomberg and Cone.[4] Following the same line of reasoning which determined the quinol formula for the coloured modification of the unimolecular compound, these observers prepared *p*-bromotriphenylmethyl chloride, which, acted upon by molecular silver, removed not only two atoms of chlorine giving the triaryl compound, but also one atom of bromine. This could only occur if the nuclear bromine atom became attached, as in the former case, to the quinoid nucleus (indicated by an asterisk).



Moreover, Jacobson's formula explains in a simple way the action of acids on triphenylmethyl,[5] which yields a compound first obtained by Ullman and Borsum.[6]



The only other compound whose structure has yet to be considered

[1] *Annalen*, 1911, 381, 34.

[2] According to *Beer's Law* the intensity of colour in a solution is proportional to its concentration.

[3] Hantzsch, *Ber.*, 1910, 43, 3049; 1911, 44, 1772; K. H. Meyer, *Annalen*, 1911, 380, 212.

[4] *Ber.*, 1906, 39, 3174; 1907, 40, 1880.

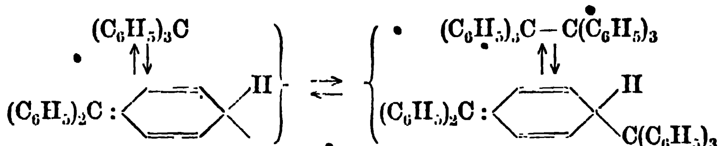
[5] Gomberg, *Ber.*, 1902, 35, 3918; 1903, 36, 376.

[6] *Ber.*, 1902, 35, 2877; Jacobson, *Ber.*, 1905, 38, 196.

is the colourless bimolecular modification which exists in the free state and in solution in equilibrium with the coloured monomolecular compound. It seems probable that it is either hexaphenylethane or an aggregate of two molecules of the tervalent radical.

The synthesis of hexaphenylethane would have settled the question, but so far all attempts to prepare it have failed. On the other hand both tetra- and pentaphenylethane have been obtained by Gomberg and Cone, who describe them as stable substances exhibiting, at least at ordinary temperatures, no tendency to absorb oxygen, or otherwise to behave as unsaturated compounds.

In conclusion, it would seem that every property of the triarylmethyl compounds may be explained by the existence of four modifications which in solution are in equilibrium. This equilibrium is represented by Gomberg[1] as follows:



Whether or not hexaphenylethane exists, or the coloured unimolecular compound possesses the quinol structure, it is abundantly proved that the bimolecular compound readily dissociates in solution, breaking up into two molecules of the triarylmethyl compound in which carbon is tervalent.

Schlenk[2] has also observed that the compound obtained by the action of sodium on aromatic ketones has the formula $(Ar)_2C.ONa$ and not the double formula (see p. 247), and the compound, formerly regarded as ditolane hexachloride, appears from recent determinations also to have half the molecular weight, and is therefore tolane trichloride $C_6H_5CCl_2.CClC_6H_5$.[3] Both compounds therefore contain tervalent carbon.

Wieland,[4] it may be added, has found that tetraphenyl hydrazine breaks up on heating into diphenyl nitride $(C_6H_5)_2N$ containing bivalent nitrogen.

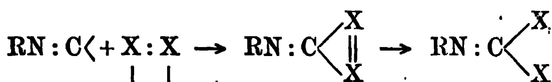
Bivalent Carbon. There are a number of compounds in which there is reason to believe that bivalent carbon is present. Among

[1] *Ber.*, 1913, 46, 228.
[2] *Ber.*, 1911, 44, 1182; 1913, 46, 2840.
[3] Löb., *Ber.*, 1903, 36, 3063.
[4] *Annalen*, 1911, 381, 200.

these are carbon monoxide, CO; fulminic acid, C:NOH; and, according to Nef, the alkyl and acyl isocyanides, RN:C, and acetylene and its halogen derivatives. Although it is possible to interpret the structure of all these compounds, except the last, as containing mutually saturated valencies by making oxygen quadrivalent or nitrogen quinquevalent, there are chemical as well as stereochemical considerations which make such a supposition improbable. If we accept the usual stereochemical arrangement of the carbon bonds, it is difficult to conceive of these four linkages being brought simultaneously into action with any other single atom. The chemical properties of most of these compounds point in the same direction.

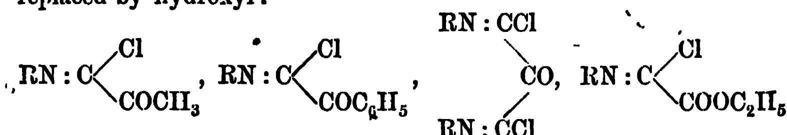
Structure of the Isocyanides. Supposing the inability of bivalent carbon in carbon monoxide to form additive compounds (except with chlorine and caustic soda) to be due to the presence of electronegative oxygen, then the replacement of oxygen by a more electropositive group might restore its additive power. Such was Nef's reasoning.[1] He selected for his inquiry alkyl and acyl isocyanides R . N:C and found that his anticipations were correct. The alkyl and acyl isocyanides form the following series of additive compounds:

1. With the halogens (Cl, Br, I) combination takes place vigorously at low temperatures. The reaction, according to Nef, proceeds in steps. The halogen molecule X_2 unites first by virtue of its residual valency and then separates into its constituent atoms.



That the halogens actually take up these positions is proved by the fact that union with amines yields guanidines.

2. With acid chlorides (acetyl, benzoyl, carbonyl, and chloroformic ester) the following are formed, in which the halogen may be replaced by hydroxyl:



3. The isocyanides unite with free oxygen, reduce metallic oxides, and combine directly with sulphur to form carbimides and thiocarbimides:

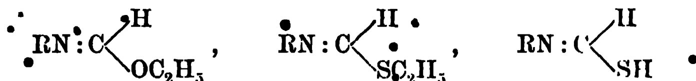


[1] *J. Amer. Chem. Soc.*, 1904, 26, 1549; *Annalen*, 1892, 270, 267; 1894, 280, 291.

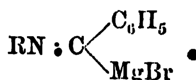
4. They combine with amines H—NHR and hydroxylamine H—NHOH:



5. They combine with alcohols, mercaptans, and hydrogen sulphide:

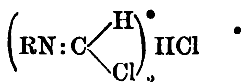


6. With phenyl magnesium bromide a compound of the formula,

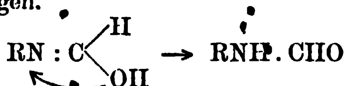


is formed.

7. In absence of water the halogen acids produce additive compounds which by analogy are represented as follows:



Moreover, like other unsaturated compounds they polymerise; thus phenylisocyanide rapidly changes to a resinous mass. Hydrolysis, on the other hand, produces the formamide RNH . CHO, from which it appears that carbon in the isocyanide had three available bonds; but the exact mechanism of the addition process is unknown, and it is quite conceivable that the elements of water first attach themselves to the carbon atom and that this is followed by the migration of hydrogen to nitrogen.



Nef further points out that many of the above reactions are reversible and the isocyanide and its addendum may dissociate at an appropriate temperature in the same manner as ammonium chloride.

There seems no reason, therefore, to doubt the existence of bivalent carbon in alkyl and acyl isocyanides.

Structure of the Metallic Cyanides. The metallic cyanides probably possess a similar structure. Like the alkyl and acyl isocyanides, alkaline cyanides readily unite with oxygen. Potassium cyanide forms potassium cyanate on oxidation and probably unites with chlorine to form $KNCCl_2$. Like the alkyl isocyanides the alkaline cyanides form double salts with the heavy metallic cyanides, whereas the few double salts of the alkyl cyanides are much less

stable.[1] A significant fact is the existence of sodium ferrofulminate $Na_4Fe(ON:C)_6 + 18H_2O$, which has been proved to contain bivalent carbon, so that sodium ferrocyanide by analogy should be written $Na_4Fe(N:C)_6$.[2] Another fact discovered by Nef also points in the same direction. Potassium cyanide and ethyl hypochlorite give ethyl cyanimido carbonate, the formation of which can only be satisfactorily explained by adopting the isocyanide structure.

$$KNC \rightarrow KNC\begin{matrix}\diagup OC_2H_5\\ \diagdown Cl\end{matrix} \xrightarrow[KCN]{} \begin{matrix}KNC.OC_2H_5\\ |\\ ClC:NK\end{matrix}$$

$$\xrightarrow[H_2O]{} HNC\begin{matrix}\diagup OC_2H_5\\ \diagdown CN\end{matrix} + KOH + KCl$$

The behaviour of silver, mercury, and certain other metallic cyanides of the heavy metals differs from that of the alkaline cyanides. They are not oxidised by permanganate and yield isocyanides with the alkyl halides, whereas the alkaline cyanides yield cyanates in the first case and mainly cyanides in the second. On the other hand, the acyl halides, such as acetyl chloride, give cyanides and not isocyanides with silver cyanide. The last fact disposes of the view that the two classes of metallic cyanides are differently constituted, the alkaline cyanides being normal and the silver and mercury compounds having an 'iso' structure. How are these observations to be reconciled? Nef considers that both classes of metallic cyanides have the iso structure and that the difference in behaviour lies in the electrochemical character of the metal. Whilst the alkaline cyanides react with the alkyl halides by direct addition to give the alkyl cyanide thus:

$$KNC + RI \rightarrow KNC\begin{matrix}\diagup R\\ \diagdown I\end{matrix} \rightarrow NCR + KI$$

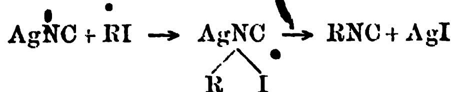
silver cyanide reacts by direct substitution:

$$AgNC + RI = RNC + AgI$$

There seems to be also some evidence that potassium cyanide forms additive compounds with alkyl iodides.

Wade[3] in a subsequent investigation, whilst accepting Nef's views as to the structure of the metallic cyanides, has given a rather different interpretation to the interaction of silver cyanide with the alkyl halide, which he represents as follows:

[1] Hofmann and Bugge, *Ber.*, 1907, 40, 1772; Ramberg, *Ber.*, 1907, 40, 2578.
[2] *Annalen*, 1894, 280, 335.
[3] *Trans. Chem. Soc.*, 1902, 81, 1603.



Thus, while addition to the alkaline cyanide with its strongly electropositive metal takes place at the carbon atom, in the case of silver cyanide with the weaker electropositive metal it occurs at the nitrogen atom. It must be admitted that neither proof appears very conclusive.

Sidgwick[1] has made the ingenious suggestion that in all cases addition to carbon takes place, and that the additive compound may exist in two stereoisomeric forms:



Formula II, corresponding to the synaldoximes, represents the additive compound of the alkaline cyanide and yields, by removal of the metallic iodide, the alkyl cyanide as formulated by Nef. The first formula (I), which represents the additive compound with silver cyanide, undergoes the Beckmann conversion, and by interchange of metal and alkyl group, followed by the detachment of the metallic iodide, yields the isocyanide.



But there is no proof whatever of any such reaction.

The Structure of Hydrogen Cyanide. The study of the structure of hydrogen cyanide, which, like the nitriles and isocyanides, may exist in two different forms, has produced evidence of such a conflicting character that it seems at present purposeless to offer more than a brief outline of the arguments for and against the one or other structure until the subject has advanced a stage. It is clear that no purely chemical method will suffice to settle the question, for reasons already given in the chapter on isomeric change (Part II, p. 313). The following facts have been advanced in favour of the nitrile structure. Hydrogen cyanide undergoes hydrolysis by alkalis which are without action on alkyl isocyanides, whereas acids which act slowly on hydrogen cyanide decompose isocyanides with great rapidity. Again, the alkyl isocyanides, like the alkali cyanides, which may be assumed to be iso compounds, dissolve silver cyanide, whilst

[1] *Proc. Chem. Soc.*, 1905, 21, 120.

nitriles and hydrogen cyanide do not. When hydrogen cyanide is heated it polymerises; but there is no evidence that it undergoes isomeric change; nitriles, on the other hand, yield isocyanides. The polymeride obtained from hydrogen cyanide forms glycosine on hydrolysis and is therefore aminomalonitrile, $NH_2.CH(CN)_2$, indicating thereby that the nitrile rather than the isocyanide has undergone polymerisation.[1] There are a large number of chemical facts which point in the same direction, such as the preparation of hydrogen cyanide from formamide [2] and formoxime [3] by dehydration, a reaction which corresponds to nitrile formation. Its additive compounds with metallic chlorides[4] resemble those of the nitriles and its stability towards ethylhypochlorite and chlorine is in marked contrast to the alkyl isocyanides[5] (p. 66). Its union with diazomethane to form acetonitrile[6] has been discounted as a fact in favour of the nitrile structure since the discovery that isocyanide is also formed.[7]

Many of the physical constants also indicate a nitrile structure; its refractivity,[8] its high dielectric constant and ionising power correspond to those of the lower nitriles.[9] Michael and Hibbert[10] take the same view and regard the true hypothetical acid as having the isocyanide structure, but from the absence of salt formation when pure hydrogen cyanide is added to trialkylamines (though the cyanides of these substances can be formed in other ways) they conclude that the actual compound is formonitrile. It is true that the primary and secondary amines do yield unstable salts, but it is contended that the union is accompanied by isomeric change, a form of argument which has an air of special pleading.

On the other hand Chattaway and Wadmore[11] adopt the isocyanide formula on account of the ease with which hydrogen is exchanged for halogen in hydrogen cyanide and its salts.



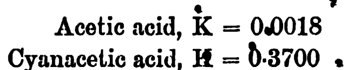
$$C:NH, \qquad C:NCl, \qquad C:NK.$$

Cyanogen chloride has the characteristic properties of a nitrogen chloride and consequently the isocyanide formula for hydrogen cyanide explains most satisfactorily its whole chemical behaviour.

The weak character of the free acid compared with the effect of,

[1] Lescœur and Rigaut, *Compt. rend.*, 1879, 89, 310.
[2] Hofmann, *Trans. Chem. Soc.*, 1863, 16, 74.
[3] Dunstan and Bossi, *Trans. Chem. Soc.*, 1898, 73, 360.
[4] Klein, *Annalen*, 1850, 74, 86.
[5] Nef, *Annalen*, 1895, 287, 274.
[6] von Pechmann, *Ber.*, 1895, 28, 857.
[7] Peratoner and Palazzo, *Atti R. Accad. Lincei*, 1907, 16, 432.
[8] Brühl, *Zeit. physik. Chem.*, 1895, 16, 512.
[9] Schlundt, *Zeit. physik. Chem.*, 1901, 5, 157.
[10] *Annalen*, 1909, 364, 64. [11] *Trans. Chem. Soc.*, 1902, 81, 192.

the cyanogen group in increasing the acidity of acetic acid (a fact which has been advanced by Ostwald as indicating an isocyanide structure),

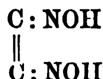


loses its force when a similar comparison is drawn between the CCl_3 group in chloroform and the same group in trichloracetic acid, the former producing a neutral non-electrolyte and the latter a strong acid with an affinity constant, K = 120·0. Nef has attributed the poisonous character and low boiling-point of hydrogen cyanide to the isocyanide structure; but it appears now that alkyl cyanides as well as cyanogen produce symptoms resembling hydrogen cyanide poisoning. In its ready formation of additive compounds, such as HCN . HCl and 2HCN . 3HCl, it appears to resemble the isocyanides; but, from their behaviour, it seems that the probable formulae are:



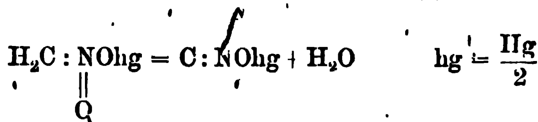
The weight of evidence appears therefore in favour of the nitrile structure; but, as stated above, chemical reactions alone are incapable of settling the question.

The Structure of Fulminic Acid.—The presence of bivalent carbon in fulminic acid has been demonstrated by Nef.[1] Mercury fulminate, which was discovered by Howard in 1800 and has since found such an extended application as a detonator, is prepared by the action of mercuric nitrate in nitric acid on ethyl alcohol. The analysis corresponds to the molecular formula $HgC_2N_2O_2$, and it is therefore isomeric with mercury cyanate. Passing over the earlier researches of Kekulé (p. 51), who regarded it as a derivative of nitro-acetonitrile, it has been shown that hydrochloric acid breaks it up into hydroxylamine and formic acid, suggesting the following formula for the acid:

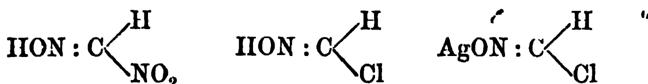


The single carbon formula C : NOH or carbyloxime has been deduced from its synthesis. Nef obtained it by the action of mercuric chloride on sodium nitromethane, which probably reacts by forming a mercuric salt of nitromethane and then loses the elements of water.

[1] *Annalen*, 1894, 280, 275, 303.



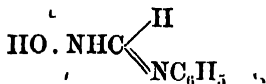
Moreover, mercury fulminate when acted on by nitrous acid is converted into methyl nitrolic acid, $(NO_2)HC:NOH$. Seeing that both nitromethane and methyl nitrolic acid contain only one carbon atom, there is strong proof of the presence of a single carbon atom in fulminic acid. The formation of methyl nitrolic acid from a fulminate and nitrous acid as well as of formylchloride oxime, by the action on the sodium salt of the former with hydrochloric acid, and the existence of an additive compound of hydrogen chloride and silver fulminate, all point to the presence of bivalent carbon.



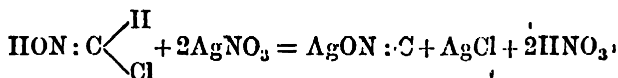
Additive compounds with hydrogen sulphide and sulphate are also known and are readily prepared.



The structure of formylchloride oxime is further determined by its decomposition, on standing, into hydroxylamine hydrochloride and carbon monoxide, and by its conversion with aniline into phenyl isouretin, the structure of which has been fully established.



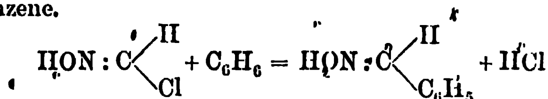
It may also be added that silver nitrite converts formyl chloride quantitatively into silver fulminate.



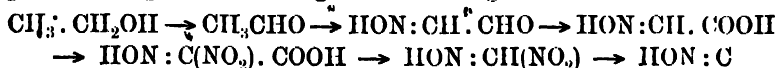
In addition to Nef's synthesis, already mentioned, fulminic acid has been obtained by Wieland[1] from methyl nitrolic acid and similar compounds, the formation of which is easily accounted for in each case by adopting Nef's formula. Scholl[2] found that in presence of benzene and a mixture of anhydrous and hydrated aluminium chloride, mercury fulminate may be converted into benzaldoxime. The reaction is most simply explained in the following way. The hydrated alu-

[1] Ahrens' *Vorträge*, 1909, 14, 385.
[2] *Ber.*, 1899, 32, 3492; 1903, 36, 10, 322, 648.

minium chloride liberates hydrogen chloride from the fulminic acid and unites with it to form formylchloride oxime, which then combines with benzene.

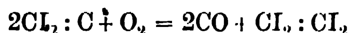


Finally, the molecular weight of the sodium salt has been ascertained by the cryoscopic method, whilst the molecular conductivity shows that the acid is monobasic, and both point to the acid possessing the unimolecular formula, C : NOH. All that remains is to briefly indicate the formation of fulminic acid from alcohol, which probably passes through the following series of changes:



The acid then unites with mercury to form mercury fulminate.

Structure of Acetylene Compounds. Nef[1] found that if dibromethylene, $C_2H_2Br_2$, is acted upon with aqueous-alcoholic soda it yields a gas, bromacetylene, C_2HBr. This substance is exceedingly reactive; it combines vigorously with oxygen, phosphoresces, gives the ozone reaction, smells like hydrogen cyanide, and is poisonous. The alkyl and acyl derivatives of acetylene, on the other hand, have a sweet smell and other properties in marked contrast to the above bromine compound. Dibromacetylene, C_2Br_2, is obtained by the action of alcoholic potash in the cold on tribromethylene. It smells like an isocyanide, and is both very poisonous and spontaneously inflammable. Moreover, it combines directly with sodium ethoxide and phenoxide to form dibromophenyl- and ethyl-vinyl ethers, $C_2Br_2H.OR$, and with hydriodic acid to form dibromiodethylene, C_2HBr_2I. The fact that all three compounds give dibromacetic acid or its ester on oxidation, taken in conjunction with the unstable character of dibromacetylene, its poisonous properties and striking similarity in smell to the isocyanides, led Nef to regard both mono- and dibromacetylene as derivatives of acetylidene, $CH_2:C\langle$, $CHBr:C\langle$, $CBr_2:C\langle$. For similar reasons, and also because diiodacetylene breaks up on oxidation into tetraiodethylene and carbon monoxide, the former is regarded as diiodacetylidene.

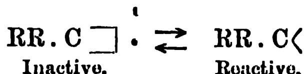


$$2CI_2:C + O_2 = 2CO + CI_2:CI_2$$

The metallic compounds are formulated in a similar fashion, $CaC:C\langle$, $Ag_2C:C\langle$, &c., and acetylene itself is represented as possessing the acetylidene structure.

[1] *Annalen*, 1897, **298**, 332; 1899, **308**, 325.

Although exception may be taken to Nef's views on the structure of the acetylene compounds, the existence of bivalent carbon in the other groups, which have been discussed, seems to be firmly established. The question whether the unsaturated valencies should be represented as mutually saturating one another, or free, or, as Nef supposes, an equilibrium mixture of both, the free being the reactive, and the combined the inactive form, does not seem to possess much real significance.



The Nature of Unsaturated Groups. By an unsaturated group, as distinguished from an unsaturated atom, we wish to imply the union of two atoms whose affinities are not saturated. When the union lies between carbon and carbon we obtain the unsaturated hydrocarbons and their derivatives. It is clear that in a case of this character, as, for example, in ethylene and acetylene, we may indicate unsaturation in several ways. Adopting Werner's view that valency may distribute itself unequally over the atom, a larger amount will be available for uniting unsaturated than for saturated carbon, or unsaturation may be indicated by the union of bivalent or tervalent carbon atoms, leaving a certain amount of affinity free, or, again, the unsaturated valencies may be represented by the method adopted by Nef in bivalent carbon compounds, as saturating one another. In the last case we obtain what are known as double or treble bonds or linkages. Although the double and treble bond is very generally accepted, it may be well to state briefly the evidence upon which it rests. We will then proceed to discuss the theory of free valencies, i.e. the union of bivalent and tervalent carbon, and finally Werner's theory in its application to unsaturated compounds.

Theory of the Double Bond. In the first place, there is nothing intrinsically improbable in the notion of a force of attraction being concentrated at definite points on the atom or having a definite direction, which may be symbolized by bonds. The view, indeed, receives substantial support from the theory of the valency electron, which is discussed later (p. 96). This theory represents valency as residing in one or more electrons which occupy a definite position in or near the surface of the positively charged atom and send out lines of force which either terminate on other atoms and so bind them or curve back on the atom from which they proceed.

But there are other grounds upon which the theory of the double bond rests. All unsaturated compounds unite with an even number

of univalent atoms or groups; in other words, the saturation of one unsaturated carbon atom necessitates that of the other, and moreover the unsaturated carbon atoms invariably adjoin one another. There is an obvious connection of a special kind between the two unsaturated carbon atoms, for which the device of the double bond is made to serve.

If ethylene and ethane differed merely in the number of hydrogen atoms attached to the two carbon atoms, we should expect the heats of combustion and formation and other physical constants to be determined solely by the presence or absence of hydrogen; but we know that this is not the case. The physical constants for unsaturated compounds are fully discussed in a subsequent chapter (Part II, chap. i), but it may be stated here that the difference between saturated and unsaturated carbon is clearly brought out in the values for molecular solution-volume, refractivity, magnetic rotation, and heat of combustion. For example, the heats of combustion of ethane, ethylene, and hydrogen given by Thomsen are:

C_2H_6	370·44	mol.-grm.-cals.
C_2H_4	333·35	„
H_2	68·36	„

If the value for ethylene were that of ethane less two atoms of hydrogen, it would be 370·44 – 68·36 = 302·08, whereas much more heat is evolved. The conclusion is that unsaturated carbon atoms are more easily severed than the saturated atoms, and less energy is consequently absorbed in the process of cleavage.

Unsaturated carbon possesses therefore a higher energy content or the carbon atoms are at a higher chemical potential than when saturated. But evidence of a more convincing kind is derived from stereochemical considerations.

Evidence of Stereochemistry. The principles of stereochemistry, enunciated by van 't Hoff (Part II, chap. iii), are based upon the relation subsisting between optical activity and the presence of asymmetric carbon in saturated compounds, and again on well-marked physical and chemical differences among the so-called geometrical isomers of the olefine series. This theory rests upon the assumption of a definite position and direction of the valency attachments. But it offers something more than an explanation of these forms of isomerism, important though they are.

We must be careful to recognize clearly that the method of indicating unsaturation by a double bond is not taken to imply a firmer connection between the unsaturated carbon atoms any more than an

increased valency value indicates additional strength of affinity (p. 56).[1] The double bond is, in short, a point of weakness in a molecule rather than of strength. Thus, on oxidation with permanganate or fusion with potash, the double link forms the point of cleavage and, as already pointed out, the heat of combustion of an unsaturated compound, atom for atom, is greater than that of a saturated compound. It contains a larger store of available energy and is consequently less stable.

Various theories giving prominence to the idea of the weakness of the double bond have been advanced, and rest mainly on the space arrangement of the carbon bonds. If we suppose the bonds to diverge at equal angles (109·5°) from the central carbon atom and to retain their positions when the two carbon atoms become doubly linked, the space arrangement viewed in perspective will appear as shown in Fig. 1.

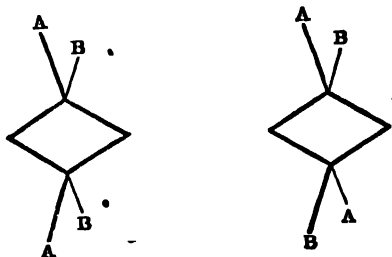


Fig. 1.

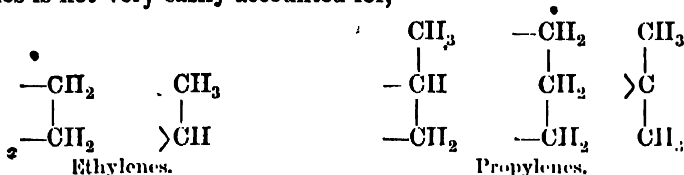
If the single bond represents the direction and measure of the force of affinity, the resultant of the two forces acting at an angle of 109·5° will not be the equivalent of the same forces acting in a straight line but very much less. According to Baeyer's *strain theory* (see p. 178), if the result of the double linking tends to bend the two pairs of bonds from their original positions into a straight line joining the two carbon atoms, a condition of strain will be set up which will occasion instability. This theory is developed more fully in connection with the formation of cyclic compounds (p. 178); but it may be mentioned here as a significant fact that the ring systems which occasion least deformation in the normal arrangement of the bonds contain five and six atoms, and of all ring systems these appear to be the most readily formed, the most stable, and of the most frequent occurrence in nature. Without, therefore, a definite position and direction of the

[1] It is for this and other reasons that some chemists, notably Lossen (*Annalen*, 1880, 204, 295), Hinrichsen (*Ueber den gegenwärtigen Stand der Valenzlehre*), and Werner (*Neuere Anschauungen auf dem Gebiete der anorganischen Chemie*), have refused to accept this method of denoting unsaturation.

force of affinity, the theory of stereochemistry in its relation to stereoisomers and ring formation would have to be modified, if not relinquished.

The Theory of Free Valencies. The theory of free valencies, which was at one time adopted by Fittig to explain the isomerism of maleic and fumaric acid, has been recently revived by Hinrichsen,[1] who considers that the nature of unsaturation of ethylene compounds in no way differs from that of compounds containing bivalent carbon (p. 65). They form additive compounds with the same class of reagents and under similar conditions, and therefore, if substances like carbon monoxide, the isocyanides, fulminic acid, and triphenylmethyl contain free valencies, there is no reason why ethylene should be denied this attribute.

It is true that the non-existence of isomeric ethylenes and propylenes is not very easily accounted for,



but the absence of the radical CH_3 Hinrichsen regards as no more remarkable than that of PH_2 or NH_4. As the electrochemical character of elements becomes more emphasized in their lower valency combinations without having recourse to multiple linkages (e.g. chlorine in HCl is more electronegative than in ClO_2), so the electronegative character of unsaturated carbon is accentuated in acetylene, in which hydrogen is replaceable by metals, and multiple linkage may be equally dispensed with.

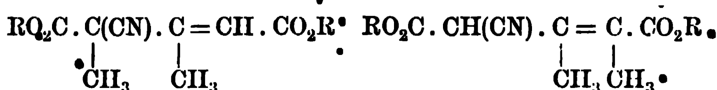
Stereoisomerism, which might present a difficulty, is explained by adopting Knoevenagel's view[2] of the constitution of carbon compounds in which carbon and attached atoms or groups in saturated compounds occupy the faces of the tetrahedron and not the points, whilst in ethylene compounds the two tetrahedra are pivoted on an edge and oscillate backwards and forwards, addition taking place on opposite faces at the extreme of an oscillation on one side or the other. In opposition to this view it is contended that if a comparatively stable compound like ethylene possesses free valencies, there is no reason why, for example, an isomeric propylene $\overset{|}{C}H_2 . CH_2 : \overset{|}{C}H_2$ should not exist.

Now although the balance of evidence would appear to favour the

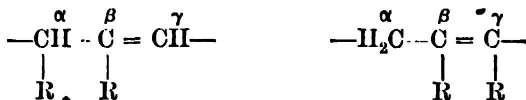
[1] *Annalen*, 1904, 336, 223. [2] *Annalen*, 1900, 311, 194.

existence of double bonds in unsaturated compounds, nevertheless certain recent observations have been recorded which seem capable of no other simple interpretation than the assumption of free valencies.

The facts are briefly as follows: in 1905 Thorpe and Rogerson[1] obtained two esters having entirely distinct properties, to which the following formulae were assigned:



The two esters on hydrolysis yielded one and the same αβ-dimethylglutaconic acid, that is, the two groupings are identical.



Identity was also found to exist in the following pairs: α- and γ-methylglutaconic acids and the α-methyl-γ-ethyl and α-ethyl-γ-methyl-glutaconic acids. In other words, the α and γ positions are identical, no doubt for the same reason that determines the equality of the two meta positions in the benzene ring and the identity of compounds described under virtual tautomerism (Part II, p. 327).

Two explanations might be given of the cause of this identity in the α and γ positions: a dynamical one, based on the assumption that the free hydrogen atom oscillates between the α and γ positions with recurrent change of linkage, or a statical one, in which the atomic arrangement is fixed and symmetrical, a condition which would involve the conception of free valencies of the end carbon atoms or, what amounts to the same thing, the presence of two tervalent carbon atoms.

The two views may be expressed thus:



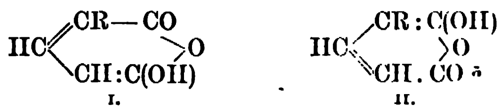
In 1909 Feist[2] prepared a second and labile α-methylglutaconic acid which at first sight points to the existence of cis- and trans-isomerism and was so regarded by its discoverer, and the fact appeared to be confirmed by the preparation of other α- and β-monoalkyl, αβ- and αγ-dialkyl-, and αβγ-trialkyl-glutaconic acids in isomeric forms.[3] Were this a case of geometrical isomerism, it would dispense at once with both the foregoing explanations.

[1] *Trans. Chem. Soc.*, 1905, 87, 1669, 1685. [2] *Annalen*, 1909, 370, 41.
[3] Thorpe and Thole, *Trans. Chem. Soc.*, 1911, 99, 2187.

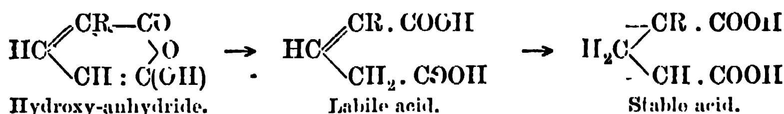
The inadequacy of the stereoisomeric explanation has been placed in a very clear light by Thorpe and his collaborators. α-Alkylglutaconic acid may be taken as a typical case. It is converted on treatment with acetyl chloride into an anhydride, which acts as a monobasic acid. It forms well-crystallised alkali salts from which acids liberate the original anhydride; it yields an acetyl derivative, and with phosphorus chloride, hydroxyl is replaced by chlorine.

When hydrolysed with strong potassium hydroxide solution or by dilute alkali carbonate in presence of casein[1] the anhydride passes into the salt of the labile acid, which is rapidly converted by boiling with hydrochloric acid into the stable acid.

The process of formation and acid properties of the anhydride point unmistakably to one of the following formulae:



that is, the free hydrogen atom of the three-carbon system passes to the oxygen, forming a hydroxyl group. Of the two, the first formula is preferred owing to the absence of pyruvic acid among the products of oxidation, which the second might be expected to yield. Now in the conversion of the alkali salt of the hydroxy-anhydride into the salt of the labile acid and the latter into the stable acid, the following changes will, according to Thorpe, occur:



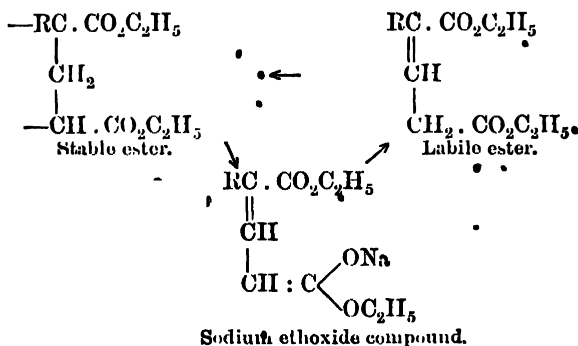
The different alkylglutaconic acids examined appear to behave much in the same way, and differ mainly in the stability of the hydroxy-anhydride and the labile forms of the acids which are greatly influenced by the position of the alkyl group. Glutaconic acid itself, though it gives a hydroxy-anhydride, forms no labile isomer. But what evidence is there for the existence of two structural rather than of two geometrical isomers?

The evidence is briefly as follows:[2] glutaconic ester and its alkyl derivatives containing a mobile hydrogen atom, when treated with sodium ethoxide, give yellow sodium ethoxide compounds. When

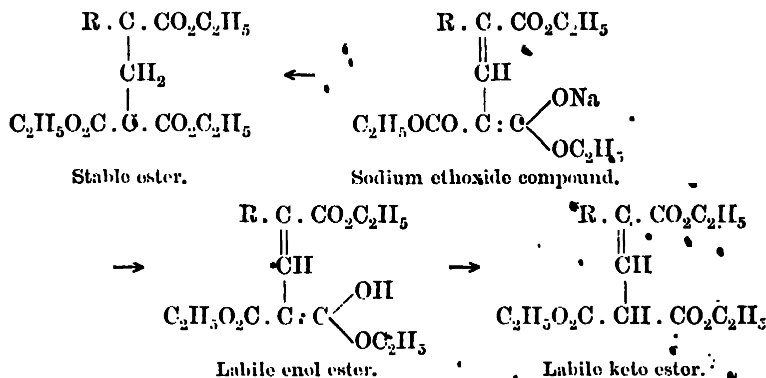
[1] Casein in small quantity acts as an 'anticatalyst'. After treatment with dilute alkali the acid is converted into the silver salt from which H_2S liberates the labile acid. With strong potash the dipotassium salt of the labile acid is formed.

[2] Thorpe and Bland, *Trans. Chem. Soc.*, 1912, 101, 871.

the sodium compound is decomposed by water the first product according to Thorpe must be the ester of the labile acid, a portion of which, according to the varying stability of the acid, would pass into the stable ester.



The two esters cannot however be distinguished, since they are both insoluble in alkaline solution. But by introducing two negative groups into the group carrying the acid hydrogen, the sodium compound is thereby rendered more stable in aqueous solution and can be separated from the normal ester produced at the same time by extracting the latter with ether.



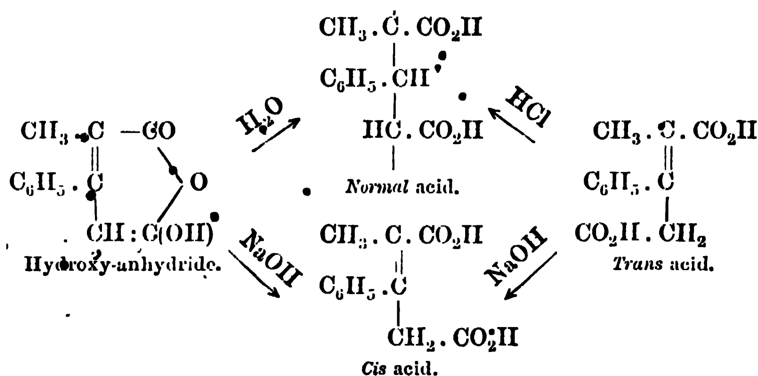
From the sodium compound which is present in the enolic form carbon dioxide liberates the labile ketonic compounds. The above process has been carried out in the manner described with the

carbethoxy-derivatives of α-methyl, ethyl, and benzyl-glutaconic esters and in each case a labile ester was isolated in enol and keto forms which underwent conversion into the stable ester.

The discovery of a third isomer of β-phenyl-α-methylglutaconic acid has afforded the final proof of Thorpe's view.[1]

In the process of synthesizing the ester, two forms were obtained, a liquid and a solid, corresponding probably to the *cis* and *trans* isomer (see Part II, p. 243). When the liquid ester is hydrolysed it yields two acids which, according to Thorpe, represent the *normal* and *cis* acids, whilst the solid ester only gives one product.

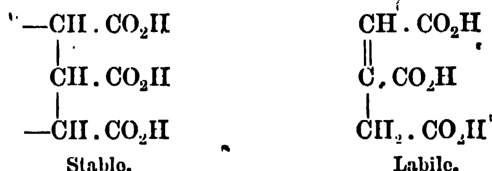
If the hydroxy-anhydride, obtained as previously described, is boiled with water, it is converted into the *normal* acid: if treated with concentrated alkali, it forms a mixture of the *normal* and *cis* acids; finally, if acted on with dilute alkali in presence of casein, only the *cis* acid is obtained. Again, the *trans* acid may be converted into the *cis* acid by the action of alkali, whilst the latter passes into the hydroxy-anhydride with acetyl chloride. So far no method has been devised for converting the *cis* and *normal* acid into the *trans* modification. This close connexion between the three compounds is further illustrated by the fact that all three, when boiled with mineral acids, give the same isobutenylbenzene, $CH_3.CH:C(C_6H_5)CH_3$.



A very similar series of experiments conducted by Thorpe and

[1] Thorpe and Wood, *Trans. Chem. Soc.*, 1913, 103, 1569.

Bland[1] on aconitic acid has revealed the existence of stable and labile forms of this acid, which the authors represent by the following formulae:



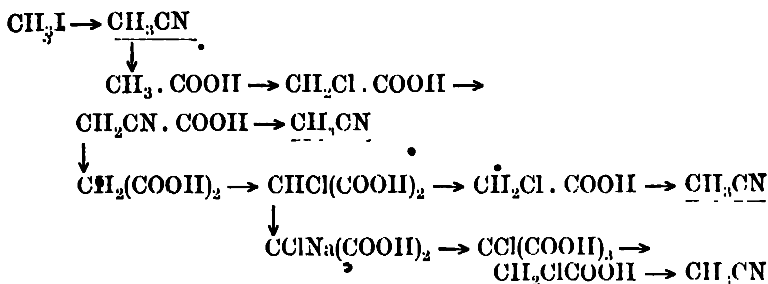
In this case the labile acid is a comparatively stable substance, which differs from the normal acid in its melting-point and in its behaviour with acetyl chloride. Whereas pure acetyl chloride free from phosphorus chloride gives no anhydride with the ordinary acid, the labile modification is converted by both the pure and impure reagent. No attempt, it seems, has been made to determine the nature of the bromine addition products.

Werner's Theory of Unsaturation. This theory, which is discussed on p. 90 in connection with Werner's theory of valency, represents the force of affinity as emanating from the centre of a spherical atom and distributing itself evenly over the surface. The distribution may, however, change according to the nature of the attached atoms. In methane, where the atoms linked to the central carbon atom are the same, the amount of valency is evenly distributed among the four hydrogen atoms. In the case of a substance such as ethylene, the attached carbon atoms command a certain larger share of affinity. This larger share of affinity would appear at first sight to have the effect of binding the unsaturated carbon atoms more firmly than the smaller amount demanded by the saturated atoms. The explanation of this apparent paradox is given on p. 86. The phenomenon of geometrical isomerism as explained by Werner's theory has been discussed at length in Part II, p. 258. There only remains the application of the theory to ring structures, and it must be confessed that this is its weakest point. Werner's theory affords no satisfactory explanation of the peculiar stability of five- and six-atom rings; on the contrary, the very reverse effect would be anticipated, that is to say, the carbon atoms when most closely in contact and whose affinities would therefore be most completely neutralised, should offer the greatest stability, and this would necessarily exist in the smaller and not the larger ring formations.

[1] *Trans. Chem. Soc.*, 1912, **101**, 1490.

Equivalence of the Carbon Bonds. An attempt has been made to establish the equal value of the four carbon valencies by a method which consists in replacing successively the different hydrogen atoms of marsh gas by the same element or group and comparing the products in each case on the assumption that during interchange of constituents no migration occurs. Henry[1] succeeded in converting methyl iodide into methyl cyanide by four different methods, and in such a manner that a different atom of hydrogen in the original compound was replaced.

The following scheme, which need not be described in detail, will indicate the nature of the process:



$CH_3I \rightarrow CH_3CN$
$\downarrow$
$CH_3.COOH \rightarrow CH_2Cl.COOH \rightarrow$
$CH_2CN.COOH \rightarrow CH_3CN$
$\downarrow$
$CH_2(COOH)_2 \rightarrow CHCl(COOH)_2 \rightarrow CH_2Cl.COOH \rightarrow CH_3CN$
$\downarrow$
$CClNa(COOH)_2 \rightarrow CCl(COOH)_3 \rightarrow$
$CH_2ClCOOH \rightarrow CH_3CN$

Equivalence determined in this way does not necessarily imply that each of the residual hydrogen atoms retains its original value after substitution has taken place, that is, keeps its original properties. In all probability quite the contrary is the case and, according to the nature of the substituent, the remaining hydrogen atom or atoms become more or less mobile, or, to put it broadly, every new substituent changes the character of the molecule.

Theories of Valency. We will conclude this account of the valency of carbon by a brief summary of the more common theories of valency.

The recognition of different degrees of affinity in the formation of compounds of definite composition runs through the whole history of modern chemistry. It appears in Berzelius' electrochemical theory applied to compounds of the first, second, and third order, when, for example, a metal combines with an oxide, a basic with an acid oxide, and, finally, when two metallic salts unite to form alums and other double salts (see p. 6), and it is clearly brought out in the principal and auxiliary valencies of Werner (p. 90), in the normal and contra-valencies of Abegg and Bodländer (p. 58), and in

[1] *Compt. rend.*, 1887, **104**, 1106; *Zeit. physik. Chem.*, 1888, **2**, 553; *Bull. Acad. roy. Belg.*, 1906 (3), **12**, 644; **15**, 333; see also E. Fischer and Brieger, *Ber.*, 1915, **48**, 1517.

the partial and residual valencies of other writers. The designation of unit of valency by a bond has, moreover, proved so serviceable in organic chemistry as to become an almost indispensable system in expressing the structure of compounds. If it is once admitted that valency may vary in strength as well as in number, the way is open for the creation of a variety of kinds of linkage. Recent years have witnessed the introduction of centric and zigzag bonds and dotted or partial valencies to denote affinities of a special kind. These symbols, it is true, are only used to interpret certain phenomena; but they tacitly imply a difference in the nature of the force of affinity for which there appears to be no sufficient justification.

The theories of valency may for convenience be divided into those which are associated with certain physical properties, those which serve to explain the character of the phenomenon, and those, mainly electrochemical, which attempt to define the cause.

Valency and Physical Properties. Mendeleeff and Lothar Meyer showed that valency and physical as well as chemical properties were periodic functions of the atomic weight of the elements. The relation of valency to atomic volume in compounds has been further developed by Barlow and Pope, Le Bas and Richards, whilst Traube has attempted to establish its connection with refractivity. Barlow and Pope[1] suppose that each atom occupies a certain space or 'sphere of influence'. These units form aggregates which constitute the chemical molecule, and in a solid the crystal form is determined by the closest possible packing of the aggregate spheres. The underlying principle of the theory is that the volumes of these spheres are determined by and proportional to the fundamental valencies of the atoms, and may be called the *valency volumes*. Thus, atoms of equal valency volume may replace one another without changing the predominant character of the crystal form, although variations in the ratio of the axes may occur.

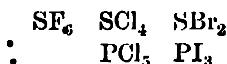
A similar theory has been propounded by Le Bas,[2] who has shown that the molecular volume at the melting-point of a series of paraffins divided by the total valency of the atoms gives a mean value of 2·97. This represents the unit valency volume. Now the difference in valency value between each member of the series is 6, that is, the valency value of CH_2, and consequently the valency volume is $6 \times 2{\cdot}97 = 17{\cdot}82$, whereas the mean difference in molecular volume actually observed is 17·83 and is, therefore, in complete accord with the theoretical value. The fundamental idea is not new. Similar

[1] *Trans. Chem. Soc.*, 1906, 89, 1675.
[2] *Trans. Chem. Soc.*, 1907, 91, 112; see also Part II, p. 6.

views were advanced by Kopp from observations on the atomic and molecular volumes, and also by Schroeder, who introduced the idea of unit atomic volume or *stere*. Traube[1] has also pointed out that the atomic refractivities for the H_α line for C, N, O. and H is in the ratio of 4 : 3 : 2 : 1. If the unit valency value is 0·787, then the molecular refractivity should be this number multiplied by the number of valencies. Normal pentane with 32 valency units has a $M_\alpha = 25·32$, equal to that of valeric aldehyde $M_\alpha = 25·31$ with the same number of valency units.

Richards[2] regards the atoms as mutually compressing one another either by force of attraction or by cohesion, and has determined the diminution of volume which liquids and solids undergo by compression. On the assumption that in both physical states the atoms are closely packed, he attributes the amount of the compression to the diminution of space occupied by the atoms themselves, and not to that of the intervening spaces. There are, consequently, two forces which determine this compression, namely, cohesion and attraction, and he explains in this way the tetrahedral form of the asymmetric carbon atom by the unequal compression produced by the four different groups on the surface of the atom.

Theories of Valency (Werner's Theory[3]). Werner's theory of valency possesses the attribute of simplicity. According to this view, which is based upon that of Claus,[4] valency is a property of attraction which emanates from the centre of an atom and is evenly distributed over the surface. The shape of the atom is of no moment as it is in constant motion, but it may be regarded as spherical. In the union of an atom with the maximum number of other atoms, the latter will distribute themselves so as to produce the greatest neutralisation of their reciprocal affinities and the surface attraction will divide itself among the atoms according to their nature. The most stable arrangement will be that in which the largest surface of the central sphere is covered without overlapping. This is taken to explain the difference in maximum valency manifested by sulphur and phosphorus in their union with the halogens, the lighter halogen atoms being present in largest number.



$$SF_6 \quad SCl_4 \quad SBr_2$$
$$PCl_5 \quad PI_3$$

It accounts also for the existence of triphenylmethyl, but not of

[1] *Ber.*, 1907, 30, 723. [2] *Trans. Chem. Soc.*, 1911, 99, 1201.
[3] *Neuere Anschauungen auf dem Gebiete der anorganischen Chemie*, by A. Werner. Vieweg, Brunswick, 1909.
[4] *Ber.*, 1881, 14, 432.

CH_3, for in the former the heavier group, like the heavier halogen, appropriates more valency. If all the four atoms attached to carbon are similar, as in methane, they will monopolize an equal amount of surface-attraction and arrange themselves in the form of a regular tetrahedron. If some of the atoms are different the distribution of affinity will be irregular, and if all four are different an asymmetrical tetrahedral grouping will result.

Werner applies his theory to the union of two carbon atoms in the following manner. The full force of affinity will only be exerted at the points of contact of the two carbon atoms, and at every other point on the hemispheres the strength of affinity will be the resultant of the force emanating from the centre and parallel to the line joining the centres of the two spheres. In Fig. 2 the force of affinity at the point where the dotted line meets the circumference of the

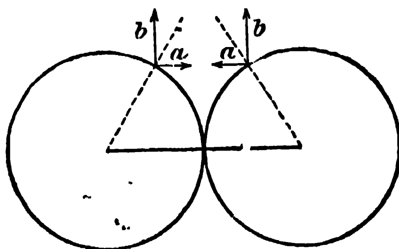


FIG. 2.

sphere may be resolved into the two forces *a* and *b*, of which only *a* will be active in binding the two carbon atoms.

The force gradually falls away as the distance between the surfaces increases, thus leaving an amount of free affinity which has been estimated at less than one-half and more than one-third of the total affinity required for binding the other atoms.

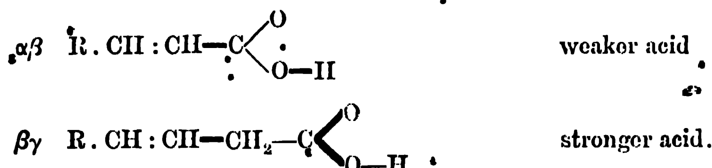
The case of unsaturated carbon has already been dealt with (pp. 59, 65), and in this case the amount of free affinity is calculated as nearly equivalent to that which is bound. By a similar disposition of two spheres Werner represents trebly-linked carbon in the acetylene series; but as only one other atom is attached to each sphere the amount of affinity left for binding the two carbon atoms is greater than that used for either a singly- or doubly-linked system. It thus appears as if more affinity were employed in joining unsaturated carbon atoms than those in which there is a single linkage. To explain this apparent paradox Werner draws a distinction between stability and reactivity. This reactivity is determined by the amount

of the component *b*, Fig. 2, which is larger in ethylene and acetylene than in ethane derivatives,[1] and serves to attach other atoms, thus rendering the unsaturated compound more sensitive to chemical action. On the basis of this general conception Werner has elaborated a theory which explains among other things those complex structures commonly known as molecular compounds. As the application of these principles is mainly concerned with inorganic compounds we have given a brief summary of the latter on p. 90.

The idea of a maximum of disposable affinity which may be differently distributed according to the nature of the union has been utilized by Flürscheim[2] to explain certain apparent anomalous affinity constants among the organic acids and bases. The theory has been embodied in the following proposition: 'The strength of a chemical bond is a function of the disposable amount of chemical force in atoms and also of the polar nature of that force.' It is found, for example, that the unsaturated aliphatic acids have the following values for K:

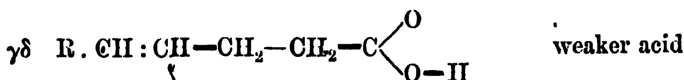
	K		K
Valeric acid	0·00165	n. Hexoic acid	0·00116
$\alpha\beta$ Pentoic ,,	0·00118	$\alpha\beta$ Hexenic ,,	0·00189
$\beta\gamma$,, ,,	0·00345	$\beta\gamma$,, ,,	0·00261
$\gamma\delta$,, ,,	0·00209	$\gamma\delta$,, ,,	0·00171
		$\delta\epsilon$	0·00191

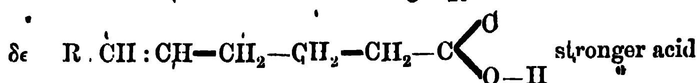
It is not obvious why the $\beta\gamma$ acid in the above series should have the highest value or why the second and fourth member in the second series should be higher than the first and third; but if the distribution of affinity, as determined by electrochemical relations, is taken into account, the reason is plain. For according to Flürscheim the strength of the acid is determined by its affinity constant or the mobility of the hydrogen atom or, in other words, by the weakness of its attachment or that of the electron (see p. 96) to the oxygen of the carboxyl group. The double bond does not utilize the full measure of two whole valencies of the atoms involved, which are consequently able to part with an extra share to the adjoining atoms. If the distribution is represented by thin and thick lines the formulae will take the following form:



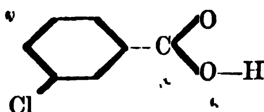
[1] *Ber.*, 1906, 39, 1278.

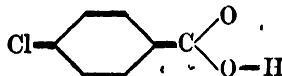
[2] *Trans. Chem. Soc.*, 1909, 95, 718; see also Meerwein, *Annalen*, 1919, 419, 123.





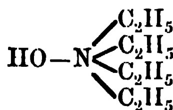
The same idea may serve to explain why the meta-, chloro-, and bromo-benzoic acids have a higher affinity constant than the para compounds.

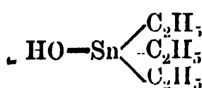




K = 0·0155 K = 0·0093

Similarly tetraethylammonium hydroxide is a stronger base than triethylstannic hydroxide, for the affinity between the electronegative nitrogen and the electropositive alkyl groups is stronger than that of tin. Hence ionisation takes place more readily in the former case.



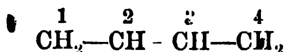


Tschitschibabin[1] shares the general ideas of Werner and Flürscheim, and like them discards the theory of multiple bonds. He distinguishes between valency or maximum combining capacity and atomicity or actual binding capacity (Bindefähigkeit), which may be anything less than the maximum, and being graduated cannot have a definite value nor be indicated by bonds. In unsaturated compounds, such as ethylene, carbon is triatomic, in acetylene and carbon monoxide it is monatomic. The more atoms the original atom can attach, the more saturated it is, the various degrees of unsaturation depending partly upon the degree of unsaturation of the attached atoms, partly on the mass of the attached radicals, and partly on the opposite electrochemical character of the two.

That the degree of unsaturation varies is shown by the varying value of the heat of combustion of the unsaturated carbon in ethylene compounds[2] and their very different affinity for bromine, &c., as shown by Bauer (see p. 116).[3] Triatomic carbon in ethylene by being joined to triatomic carbon would be more saturated than methyl; in the same way triatomic carbon is more saturated by being

[1] *J. prakt. Chem.*, 1912, 86, 381.
[2] Swientoslawsky, *Zeit. physik. Chem.*, 1909, 65, 513.
[3] Bauer, *J. prakt. Chem.*, 1905, 72, 206.

joined to two triatomic groups than to one. In butadiene the carbon atoms 2 and 3 are more saturated than 1 and 4.



$$\overset{1}{CH_2}—\overset{2}{CH}-\overset{3}{CH}—\overset{4}{CH_2}$$

In diphenylbutadiene the atoms 1, 4 being attached to heavier radicals are more saturated than 1 and 4 in butadiene, and so forth. On this principle a number of interesting facts are explained, such as Thiele's rule (see p. 133) and the existence of triphenylmethyl, the stability of which is ascribed to saturation produced by the attachment of the central carbon to three heavy radicals by the three triatomic carbon atoms of the benzene nuclei.

The theory also accounts for the saturated character of benzene, since the system consists of triatomic carbon atoms which produce a high degree of mutual saturation. It explains also the unsaturated nature of tetrahydrobenzene and also the greater unsaturation of the α as compared with the β and central carbon atoms in naphthalene, and consequent greater reactivity of the former, for the two central carbon atoms are each joined to three triatomic carbon atoms, whilst the β carbon atoms are joined to two. The α carbon atoms, on the other hand, are linked to one ordinary triatomic carbon and to one central carbon atom, which, being highly saturated, cannot greatly increase the saturation of the α carbon, which is the least saturated of the three. The theory also serves to explain the rules of substitution in aromatic compounds, and is referred to on p. 149.

But it takes little account of stereoisomerism, the essence of which lies in the definite geometrical relations of the attached atoms or groups round the central carbon atom or atoms, for which, if for no other purpose, the mechanical device of bonds has proved so fertile, nor of the nature of ring structure, which, as already stated, requires a definite disposition of the carbon valencies.

Wunderlich,[1] whose views bear an outward resemblance to those of van 't Hoff, represents the carbon atom as a tetrahedron circumscribed round a sphere; but the points of attraction are conceived as concentrated at the centres of the four faces, so that a singly linked atom will be attached to the face and not to the corner of a tetrahedron. In this way the stability of the single bond will correspond to its geometrical form.

In unsaturated compounds the carbons are represented, as in van 't Hoff's arrangement, by the edges of two tetrahedra, but in consequence of the points of attraction being situated at the centre of the tetrahedral faces, the forces joining the two carbon atoms $a\,a_1$ (Fig. 3)

[1] *Konfiguration organischer Moleküle*, Würzburg, 1886.

will be the resultant of the two pairs of forces bc and b_1c_1, leaving a residue of affinity de and d_1e_1, which may correspond to Thiele's partial valencies (see p. 133).

A similar view has been adopted by Knoevenagel, and has already been referred to (p. 77).

Werner's Theory of Valency[1] (Molecular compounds). As we have seen in a previous section (p. 82), Werner regards the valency of each atom as distributing itself according to its spatial arrangements and its degree of affinity towards contiguous atoms. Compounds are thus formed of *the first order*, which do not necessarily exhaust the amount of affinity at the disposal of the atoms in question. This residual valency can attach other atoms, and so form compounds of *the second order*. In developing this conception Werner has introduced the terms *principal* and *auxiliary* valencies to denote the above two kinds of attachment. The principal valencies correspond to our ordinary valencies and bind together atoms or groups whose saturation capacity may be measured in terms of hydrogen atoms. Such principal valencies are present in

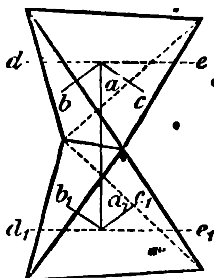


FIG. 3.

$-Cl$, $-Na$, $-NO_2$, $-CH_3$, &c.

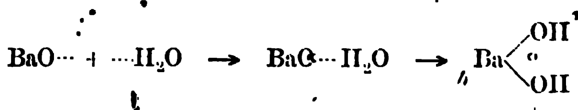
The auxiliary valencies, which are expressed by dotted in place of straight lines, represent residual affinities and link together radicals which can function as separate molecules. Such, for example, are:

$\cdots OH_2$, $\cdots NH_3$, $\cdots ClK$, $\cdots CrCl_3$, &c.

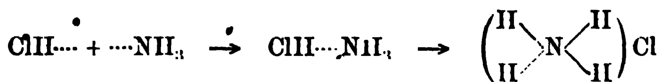
The two kinds of valencies are differentiated by their energy content, the principal valencies having a greater affinity than the auxiliary. The difference is, however, one of degree and determined by the degree of saturation of the other valencies. There is, in short, no definite line of demarcation between the two, but they merge and, under certain conditions, pass into one another, the auxiliary becoming principal and the principal auxiliary valencies.

For example, the metal and oxygen in the oxides of the alkalis and alkaline earths are united by principal valencies and form stable oxides, but nevertheless combine by their auxiliary valencies with water or alcohol, forming well-defined and stable hydrates and alcoholates, in which the OH and OR groups are linked by principal valencies.

[1] *Neuere Anschauungen auf dem Gebiete der anorganischen Chemie*, by A. Werner. Vieweg, Brunswick, 1909.



In the same way ammonium chloride is formed by union of the auxiliary valencies of ammonia and hydrogen chloride.



The formation of methylammonium iodide is produced in a similar fashion.



The position of the halogen outside the bracket is intended to indicate a difference in its attachment and to show that it is ionised in solution, as explained below.

The sulphides of arsenic, antimony, &c., combine by their auxiliary valencies with alkaline sulphides, forming sulpho-salts of considerable stability; and platinum, palladium, and gold chloride form well-characterized salts with alkaline chlorides. Some compounds, indeed, increase in stability by saturation of their auxiliary valencies. Ferric anhydride is stable in the ferrates; certain persalts are stable, containing oxides which cannot be isolated; manganese tri- and tetra-chloride are not obtainable in the free state, but readily form double chlorides and so forth.

From some of the above examples it will be seen that the number of principal valencies is not a fixed quantity, but depends on the nature of the attached atoms. With the change in number there is a change in strength, and a consequent variation in the strength of the valency. There is, however, a maximum number of principal as well as of auxiliary valencies. Werner admits that the distinction between the two kinds is of a somewhat vague and indeterminate character, and is maintained 'because it seems necessary in the present transitional state of our views on valency to mark out well-defined areas on which a more comprehensive theory may afterwards be erected'.

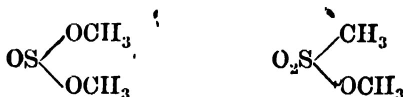
Before, however, concluding this account of the nature of principal and auxiliary valencies it should be pointed out that among the characteristics of radicals united by principal valencies is their power of functioning as independent ions, whereas those combined by auxiliary valencies lack this property. The difference may be illustrated in the case of copper glycocoll,



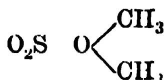
in which the copper forms an inner complex salt by means of its auxiliary valency so that in solution it does not undergo ionisation, whereas the same metal attached by a principal valency (as in copper acetate) is electrolytically dissociated. According to the electronic theory the atoms bound by principal valencies are characterized by the mobility of their electrons, a feature which is absent in those radicals which are attached by auxiliary valencies. Werner does not, however, regard the two characteristics of principal valency attachment and electrochemical behaviour as necessarily interwoven, but only in so far correlated that the saturation of the affinity simultaneously loosens the electron from the positive atom and so allows it to transfer itself to the negative component of the salt. But the saturation of a principal valency is not always sufficient to produce this effect, and in many cases the saturation of auxiliary valencies is required.

The element of a group which is separated by ionisation from the rest of the molecule is usually denoted by placing it outside a bracket.

Valency Isomerism. The distinction between principal and auxiliary valencies has been made the basis of a theory of *valency isomerism*, of which the following may serve as an illustration. Two isomeric methyl sulphites have long been known, both of which are principal valency compounds:

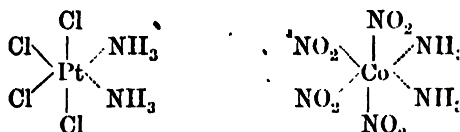


Recently E. Briner has obtained an isomeric compound in which the two parts of the compound are represented as linked by auxiliary valencies.



Without discussing at greater length Werner's views, which are mainly concerned with the constitution of inorganic compounds, we will conclude by referring briefly to the more successful application of his theory having reference to the structure of the metalammine compounds. The metal in these compounds is represented as directly linked to four or more, commonly to six, atoms or groups (NH_3, NO_2, H_2O, Cl, &c.). This number is called the *co-ordinate*

number, and is a fundamental property of the atom. The elements or groups which are directly attached to it, either by principal or auxiliary valencies, occupy what has been termed the *first zone* and do not undergo ionisation.



All those compounds in which the maximum co-ordinate number is reached are called co-ordinately saturated. In most cases the co-ordinate number is 6, but in some cases, as, for example, that of carbon, the co-ordinate number is equal to the number of principal valencies, namely 4, and this is true of the other elements in the same periodic group. The neighbouring more positive element boron and more negative nitrogen, with three principal valencies,

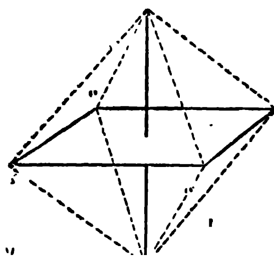


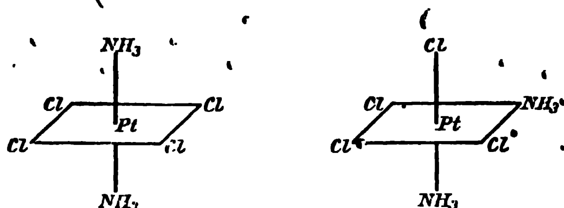
FIG. 4.

have also a maximum co-ordinate number, 4, and form compounds $HF \ldots BF_3$ and $XH \ldots NH_3$.

At an early stage in the investigation of these compounds it was discovered that substances of the above formulae, as well as many others with dissimilar radicals, existed in isomeric forms. In order to explain this kind of isomerism Werner had recourse to a space formula in which the metal occupied the centre of an octahedron and the atoms or groups the six solid angles. By this device, that is, by a different space distribution of the six groups, isomerism can be readily explained.

Four of the groups will lie in one plane and the others in a plane

at right angles. The isomerism of the two platinum compounds will appear as follows:

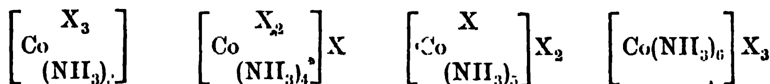


In addition to this first zone of non-ionisable groups, there exists a second or ionisable zone. For example, the following series of cobalt-ammines are known, in which X stands for an acid radical (Cl, NO_2, &c.).



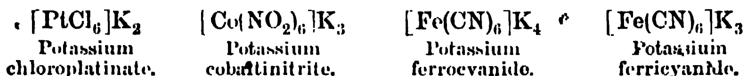
$CoX_3 + 3NH_3$ $\quad$ $CoX_3 + 4NH_3$ $\quad$ $CoX_3 + 5NH_3$ $\quad$ $CoX_3 + 6NH_3$

In the second, third, and fourth compounds of this series the substances are ionised, and it has been shown that the number of ionisable acid radicals is respectively one, two, and three. This is indicated by placing the latter in a second zone outside the bracket, thus:



$\left[Co \begin{matrix} X_3 \\ (NH_3)_3 \end{matrix}\right]$ $\quad$ $\left[Co \begin{matrix} X_2 \\ (NH_3)_4 \end{matrix}\right]X$ $\quad$ $\left[Co \begin{matrix} X \\ (NH_3)_5 \end{matrix}\right]X_2$ $\quad$ $\left[Co(NH_3)_6\right]X_3$

The outer zone is not restricted to radicals; for with an accumulation of acid radicals in the inner zone, the outer zone may be occupied by metallic atoms, forming ionisable salts. Examples of this type are potassium chloroplatinate, potassium cobaltinitrite, and potassium ferro- and ferricyanides.

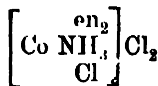


$[PtCl_6]K_2$	$[Co(NO_2)_6]K_3$	$[Fe(CN)_6]K_4$	$[Fe(CN)_6]K_3$
Potassium chloroplatinate.	Potassium cobaltinitrite.	Potassium ferrocyanide.	Potassium ferricyanide.

A remarkable discovery of isomerism among this class of substances has recently been made by Werner,[1] who has succeeded in resolving asymmetric compounds into their optically active components. Werner found at an early stage in his researches that

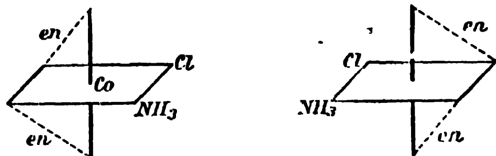
[1] *Ber.*, 1911, 44, 1887, 2445, 3132, 3272.

NH_3 could be substituted by other bases or organic amines, such as pyridine and ethylene diamine $(NH_2)CH_2 . CH_2(NH_2)$, the latter taking the place of two molecules of ammonia. The formula for ethylene diamine may be abbreviated by using the symbol *en*. A compound of the formula



$$\left[Co \begin{matrix} en_2 \\ NH_3 \\ Cl \end{matrix}\right] Cl_2$$

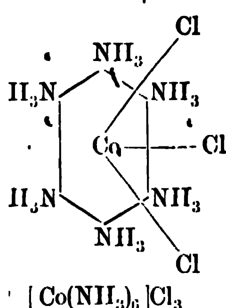
contains an asymmetric inner zone and may therefore exist in enantiomorphous forms.



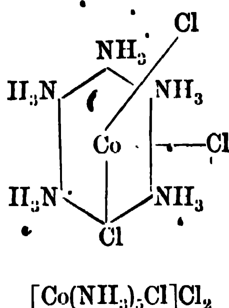
The inactive preparation has been resolved by fractional crystallisation of the *d*-bromocamphor sulphonates and then converting them into bromides (see Part II, p. 301). The enantiomorphous bromides showed a rotation of $[\alpha] = \pm 43°$, and similar results were obtained with other derivatives of cobalt, as well as with asymmetric chromium compounds.[1]

Werner's co-ordination theory is opposed by Friend[2] on the ground that the ionized atoms are so vaguely disposed as to have no definite place or definite valency in the compound, whilst the metallic atom has a valency (of six in the case of cobalt) which is contradicted in most of its simpler compounds. Furthermore, the negative atoms or groups directly attached to the metallic atom are supposed to lose their property of ionization, a fact which again is contrary to experience, at least in the simpler compounds. To overcome these difficulties Friend has had recourse to the common valency values of the atoms, and regards cobalt and platinum in the metalammines as being directly united to the negative atoms, whilst the ammonia groups float in a ring or shell composed of linked nitrogen or other non-ionized atoms round the central metallic atom. Thus cobalt hexammine trichloride and cobalt chloropentammine dichloride are represented thus:

[1] *Science Progress*, 1919, p. 253.
[2] *Trans. Chem. Soc.*, 1916, 109, 715.



$[Co(NH_3)_6]Cl_3$



$[Co(NH_3)_5Cl]Cl_2$

The isomeric α- and β-ferrocyanides of Briggs and the α- and β ferricyanides of Locke and Edwards, referred to on p. 91, are explained by supposing the central iron atom to be united in the ortho, meta, and para positions to the nitrogen atoms of the six cyanogen groups of the ring. There would thus be three isomers, but as the ortho compound is assumed to represent the double salts 4 KCN, $Fe(CN)_2$ and 3 KCN, $Fe(CN)_3$, the meta and para arrangement are reserved for the α- and β-isomers.

There are undoubtedly difficulties connected with this theory, and Friend's views have not passed unchallenged.[1] The floating ring is not less vague than Werner's ionized groups, the optically active metalammine compounds remain unexplained, and the ring chlorine atom in the second of the above formulae is furnished with the unusual valency of three.

Electrochemical Theories of Valency. The application of electricity to the explanation of affinity and later of valency originated in the first instance in the process of electrolysis, which gave birth to the electrochemical theories of Davy and Berzelius (p. 6). Those views have in recent years taken a more concrete and quantitative form by the discovery of two correlated phenomena, the first being, that the amount of electricity carried by the ion on electrolysis is constant for each unit of valency, and the second, that it is precisely this amount which in the form of the cathode ray is conveyed by the negative corpuscle or electron. The electron may therefore be regarded as the unit of negative electricity, the mass of which has been estimated at about $\frac{1}{1700}$ of that of the hydrogen atom. The results of electrolysis led Helmholtz,[2] as far back as 1881, to connect unit electrical charge with unit of valency, a view which he expounded in his celebrated Faraday lecture in the follow-

[1] Turner, *Trans. Chem. Soc.*, 1916, **109**, 1130.
[2] *Trans. Chem. Soc.*, 1881, **39**, 302.

ing words : 'If we conclude from the facts that every unit of affinity is charged with one equivalent either of positive or negative electricity, they can form compounds, being electrically neutral, only if every unit charged positively unites under the influence of a mighty electric attraction with another unit charged negatively. You see that this ought to produce compounds in which every unit of affinity of every atom is connected with one and only one other unit of another atom. This, as you will see immediately, is the modern chemical theory of quantivalence, comprising all the saturated compounds. The fact that even elementary substances with few exceptions have molecules composed of two atoms makes it probable that even in these cases electric neutralisation is produced by the combination of two atoms, each charged with its full electric equivalent, not by neutralisation of every single unit of affinity.'

The Electronic Theory of Valency. Sir J. J. Thomson's discovery of the electron and Rutherford's interpretation of the break up of the radioactive elements has thrown a new light on the structure of the atom and many of its chemical and physical properties. From observations on the small proportion of *a* particles which are deflected in their passage through matter, Rutherford concludes that almost the whole mass of the atom is concentrated on a positively charged nucleus which is of minute dimensions compared with that occupied by the atom.[1] This nucleus, which is also associated with negatively charged electrons, is further surrounded by outer rings of electrons. The magnitude of the positive charge in excess of the negative charge of the electrons attached to the central nucleus is probably represented by the *atomic number*,[2] which, with the exception of hydrogen, is about half the atomic weight.[3]

The number of negative electrons which neutralize the excess charge of the positive nucleus is, therefore, proportional to the atomic weight. On the basis of this conception of the atom and by the aid of the quantum principle, Bohr[4] has succeeded in accounting for the numerous line spectra of both hydrogen and helium. Hydrogen, it appears, contains one positive charge and one detachable electron. In the disintegration of the radioactive atom, which is accompanied

[1] *Phil. Mag.*, 1911, 21, 669; 1914, 27, 323, 488.

[2] Van den Broek, *Nature*, 1913, 93, 373, 476.

[3] The atomic number represents the numerical order of the elements as determined by the characteristic lines of the X-ray spectrum. This spectrum is obtained by photographing the X rays given by the element when bombarded by the cathode stream in an X-ray bulb, and has been accurately mapped by Moseley (*Phil. Mag.*, 1913, 26, 1024), for thirty elements.

[4] *Phil. Mag.*, 1913, 26, 1, 476; 1914, 27, 506.

by the expulsion of α-particles (helium atoms) or β-particles (electrons), or both, it is probable that the latter emanate from the central nucleus, which will, therefore, consist of helium atoms and attached electrons. Thus, the loss of one α-particle means the loss of two positive charges or two places in the atomic number.

Thomson's Theory. Thomson describes the structure of the atom as follows[1]: 'We find that in a symmetrical atom only a limited number of such electrons can be in equilibrium when arranged on a single spherical surface concentric with the atom. The actual number which can be arranged in this way depends on the distribution of positive electricity in the inside of the atom. When the number of electrons exceeds this critical number, the electrons break up into two or more groups arranged in a series of concentric shells. This leads us to the view that the electrons in an atom are divided up into a series of spherical layers, like the coatings of an onion, separated from each other by finite distances, the number of such layers depending upon the number of electrons in the atom and thus upon its atomic weight. The electrons in the outside layer will be held in their places less firmly than those in the inner layers; they are more mobile, and will arrange themselves more easily under the forces exerted upon them by other atoms.' The existence of these layers has been proved by subjecting the elements to bombardment by cathode rays. Under this treatment each element gives out a special kind of Röntgen ray.[2] The speed of the slowest cathode particle which could excite these rays is proportional to the atomic weight, and the frequency is proportional to the square of the atomic number, which is roughly that of the atomic weight.[3] These rays are assumed to arise from similar parts, that is, from the innermost ring of electrons.

On the other hand the forces which one atom exerts on another will depend mainly on the outer belt of the more mobile electrons. Thus, the increase of number in the inner rings renders the outer ring more or less stable: in other words, the outer ring may tend to lose or gain electrons, thus converting the atom into an electropositive or electronegative element, and the number of electrons which it tends to gain or lose will determine the valency. "If these properties are recurrent after the addition of a certain number of electrons, the atoms will exhibit periodic changes in conformity with

[1] *The Atomic Theory*, by Sir J. J. Thomson, Clarendon Press, 1914.
[2] Whiddington, *Proc. Camb. Philo. Soc.*, 1910.
[3] Moseley, *Phil. Mag.*, 1913, 26, 1024.

the periodic law. Thus, the number of mobile electrons in group O is nil, that of the alkali metals is one, and so forth. When the number reaches eight the ring becomes stable and the electrons no longer mobile. The outer belt of electrons is also responsible for certain optical properties, such as refractivity and dispersive power, and such physical phenomena as surface tension, cohesion, intrinsic pressure, viscosity, ionizing power, in fact, by far the most important properties of the atom.

Thomson[1] regards valency as a tube of force emanating from a valency electron and either ending on the positive charge within the atom, when they retain their mobility, or on that of another atom, when they become fixed. When all are fixed in this way, the atom is saturated. It follows, therefore, that in a molecule, say of hydrogen, for every tube of force sent out from the electron of one atom the latter must be the recipient of a second tube of force sent out from the second atom. Thus, the atom of hydrogen must be divalent and possess one positive and one negative valency which Thomson represents by arrows:



Further, chemical compounds are divided into two classes, those which have undergone *intramolecular ionization*, that is, have lost or gained electrons in the process, or *ionic molecules*, and those which have not.

Thomson's views have given rise to various interpretations of the electronic theory of valency.

Ramsay,[2] like Stark, assumes that the electron is the binding force between the atoms in a molecule. He regards eight as the total number of electrons that an atom can hold. Thus, in ammonia the nitrogen atom which already possesses five electrons receives three from the hydrogen atoms, making a total of eight. No additional electrons can now be added unless one is removed, so that the ninth valency in ammonium chloride is negative. This view of Ramsay's on the concurrent addition and removal of an electron finds expression in Friend's *residual* or *latent valencies*,[3] the *neutral affinities*[4] of Spiegel,[4] and the *electrical double valencies* of Arrhenius.[5] They serve, among other things, to bind the atoms in the molecule of an element or two electropositive elements such as potassium hydride, whilst the ordinary valencies are utilized for linking electropositive and negative atoms.[6]

[1] *Phil. Mag.*, 1914, 27, 757.
[2] *Trans. Chem. Soc.*, 1908, 93, 778.
[3] *Trans. Chem. Soc.*, 1908, 93, 260.
[4] *Zeit. anorg. Chem.*, 1902, 29, 365.
[5] *Theorien der Chemie*, Leipzig, 1906.
[6] The electronic theory of valency is responsible for a number of highly suggestive interpretations of such processes as the affinity constants of organic

Stark's Theory.[1] According to Stark there are two kinds of electrons, fixed and movable. The fixed electrons are disposed within the positively charged sphere constituting the atom, the movable electrons lie outside the atom and at some little distance from it and are attached to it by lines of force. The movable electrons have been termed *valency electrons.* It is by means of these electrons that combination is effected between similar atoms to form molecules and between dissimilar atoms to form compounds. Lines of force pass out from the electrons to other atoms with a loss of potential energy. According to the number of these lines, attachment is weaker or stronger. Thus, atoms do not combine directly, but indirectly by virtue of their mutual attraction to the electron. A single bond will correspond to a union by means of one electron, a double bond by that of two electrons, a treble bond by three, and a free bond will be represented by an unattached electron. The existence of stereoisomerism is readily explained on the assumption that the lines of force of the valency electrons are confined to definite areas on the atom. What is the number and distribution of the valency electrons? Whilst positive valency can be determined by the number of valency electrons that an atom can lose on ionisation, the negative valency may be derived from the fact pointed out by Abegg (see below) that the sum of the maximum positive and negative valencies of any atom is eight. Thus, carbon has a valency of -4 in CH_4 and $+4$ in CCl_4, phosphorus of -3 in PH_3 and $+5$ in PCl_5, iodine of -1 in HI and $+7$ in I_2O_7.

It appears, therefore, that the greatest number of valency electrons which an atom can hold is eight. Drude, on the other hand, estimates the number of valency electrons from the positive valency of the atom, from which it follows that the smaller the negative valency, the larger the number of valency electrons.

Stark regards the difference between electropositive and negative elements as due to the greater or smaller positive charge on the atom. An electronegative atom, such as chlorine, will be one with a large positive charge and therefore able to retain a number of electrons, or attract others from electropositive atoms. An electropositive element, such as hydrogen, will, on the other hand, have a small positive charge, which requires few electrons to neutralize it, and the latter will be attracted to electronegative atoms of large positive charge.

acids, substitution in benzene, &c., in numerous papers by H. S. Fry, K. G. Falk, and W. A. Noyes, which have appeared since 1910 in the *Journal of the American Chemical Society*, and which being of rather special than general application, and to which full justice cannot be done within necessary limits of space, must be left to the reader for reference.

[1] *Prinzipien der Atomdynamik.* J. Stark. Hirzel, Leipzig, 1910.

The reactivity of both kinds of atoms will be due to the ease with which they attract or repel electrons.

An atom, such as carbon, which combines with both electropositive and negative elements, is assumed to possess four electrons, with which it is able to bind four equivalent electronegative atoms; but as the lines of force of the electrons occupy a restricted area on the atom, the lines of force of four electropositive atoms may fall on intermediate positively charged areas. It is not, however, clear why the two kinds of valency should not function at the same time, a condition which, at least in the case of carbon, is unknown. In addition to the property of causing combination, Stark, like Thomson, holds that the valency electrons are probably responsible for ionisation and the phenomenon of light absorption and other optical properties (see Part II, p. 70).

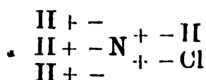
Thus the form of the positive sphere, the number and position of the electrons, and the distribution of the lines of force determine the character of the atom, that is, its affinity, valency, &c. It is by the lines of force emanating from the valency electrons that affinity is manifested and atoms are bound together in a molecule.

In unsaturated compounds it is assumed that there is a certain amount of residual affinity, that is, valency electrons whose lines of force are turned back and end on the positive spheres of the unsaturated atoms. Addition produces a fusion of the lines of force of the unsaturated atoms with those of the added atoms and consequent degradation of energy of the system. The unlocking or opening of these lines of force may be produced by adding energy to the system in various forms, heat, light, or the action of the solvent, &c.[1] This change in the energy content affecting the electrons in the molecule is manifested by the absorption of light or by the associated phenomena of fluorescence, phosphorescence, or photochemical action, referred to in Part II, p. 130 *et seq.*

Theory of Abegg and Bodländer.[2] A brief reference has already been made to this theory and the meaning which is attached to the term normal and contra-valencies (p. 58). The normal valencies are the stronger and are electropositive for metals and electronegative for non-metals. Their strength is affected by combination, which falls off as saturation proceeds. The activity of the contravalencies increases with increase in the negative character of the element and

[1] Baly, *Zeit. f. Elektrochemie*, 1911, 17, 211; *Trans. Chem. Soc.*, 1912, 101, 1469, 1475.
[2] *Zeit. anorg. Chem.*, 1899, 20, 453; 1904, 39, 330.

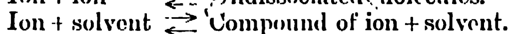
also with its atomic weight. This explains the existence of a stable oxide of iodine but not of fluorine. The activity of the contravalencies among negative elements also determines the formation of di- and poly-atomic molecules. Being latent in the metal, they possess monatomic molecules. The existence of latent contravalencies explains the formation of molecular compounds whose component molecules are similar. For when uncombined one component should contain an element belonging to the higher groups of the periodic system, and this is found to be the case. Compounds such as H_2O, NO_2, HF, $AlCl_3$, &c., and organic hydroxy-compounds, oximes, and aldehydes enter into molecular compounds. The double fluorides and chlorides, water, and alcohol of crystallisation are examples. The same reasoning accounts for ordinary molecular compounds such as $(CH_3)_2O . HCl$, $NH_3 . HCl$. In the latter case the formula will be represented thus:

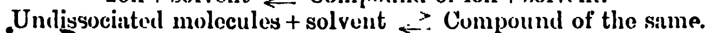


but it is improbable for reasons already given (p. 58) that the fourth hydrogen atom is combined differently from the other three. Solutions where combination of solute and solvent is indicated by thermal and other changes are placed in the category of molecular compounds. These changes are most marked when substances contain elements of high but unsaturated valency.

In electrolytic solutions the following equilibria may occur:





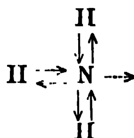


Feebly dissociating solvents are those which have no great tendency to combine with ions. If the tendency to ionisation is well developed, the affinity of the undissociated substance for the solvent is unimportant, as the non-ionised substance will not reach a high concentration compared with the ions. The case is represented by solutions of strong electrolytes whose solubility is determined by the affinity of ions for the solvent, and is therefore great in water, compared with the solubility in fully dissociated media. Sulphur dioxide, for example, is found to combine with those substances which undergo ionisation in the liquid.

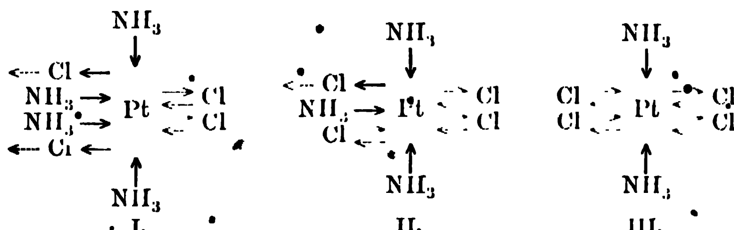
Briggs' Theory. Briggs[1] has applied Abegg's theory in order to explain the structure of the metalammine compounds. The

[1] *Trans. Chem. Soc.*, 1908, 93, 1562; 1917, 111, 253.

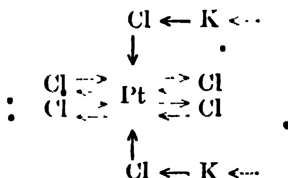
radicals do not form two zones as Werner supposes, but are all directly attached to the metallic atom by virtue of their positive and negative affinities, with which each atom is provided. For example, the platinum atom is capable of combining with six positive affinities and four negative affinities. By its positive affinities it can attach the negative affinities of four atoms of chlorine, and by its negative affinities it can attach the positive affinities of six molecules of ammonia. Ammonia has only one available positive affinity, since its other positive and negative affinities are saturated by the positive and negative affinities of hydrogen.



Chlorine has one positive and one negative affinity. The three compounds $(Pt\ 4NH_3Cl_2)Cl_2$, $(Pt\ 3NH_3Cl_3)Cl$, and $(Pt\ 2NH_3Cl_4)$ may be represented by the following formulae, in which the free affinities are indicated by dotted arrows and the combined positive and negative by arrows pointing in reverse directions.



The chlorine atoms with free affinities are those which undergo ionisation. Thus, in I two atoms of chlorine and in II one atom of chlorine are ionised, whereas III is electrically neutral. The same idea has been applied to formulating K_2PtCl_6,



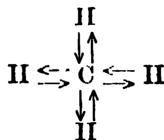
in which the two metal atoms attached to the free affinities of the two chlorine atoms undergo ionisation. Briggs has also applied

Abegg's solution equilibria, referred to above, in order to show that there will be less tendency on the part of the chlorine atoms towards ionisation by reason of the residual affinity of the water molecules when attached by two kinds of affinity than by one.

This theory has undergone a further development in the following way: It has been stated (p. 99) that J. J. Thomson recognizes two types of chemical combination producing ionic and non-ionic molecules. Bray and Branch[1] and G. N. Lewis[2] draw a similar distinction between *polar* and *non-polar* compounds. In the polar compounds (Thomson's ionic molecules) a transfer of electrons from one atom to another has taken place. In the non-polar compounds electrons have not been transferred, and the atoms are held together by equal and opposite tubes of force passing from the electrons in one atom to the positive nucleus of the other. Moreover, all gradations between a completely polar and a completely non-polar molecule are to be expected. In addition to the dual affinity of the atoms as exhibited by a tendency to both gain and lose electrons, Briggs distinguishes between primary and secondary affinity, the latter, which is opposite in sign to the former, only coming into action when the primary affinity has been saturated. In the strong electrolytes (polar compounds), such as potassium chloride, the atoms are united by primary affinity only, the secondary affinity (dotted arrow) being unsaturated, as represented by the formula:



In the non-electrolytes (non-polar compounds), such as methane, the atoms are united by both primary and secondary affinity.



Methane.

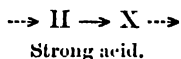
Now, copper is incapable of direct combination with ammonia molecules to give compounds of the type $Cu.xNH_3$. Cuprous chloride, however, can combine with a maximum of three molecules of ammonia to give $(Cu.3NH_3)Cl$,[3] and cupric chloride with six molecules of ammonia $(Cu, 6NH_3)Cl_2$. That is to say, the ammonia molecules are united to the copper by the saturation of the free

[1] *J. Amer. Chem. Soc.*, 1913, 35, 1443.
[2] *J. Amer. Chem. Soc.*, 1913, 35, 1448.
[3] Lloyd, *J. Phys. Chem.*, 1908, 12, 398.

positive affinity of the nitrogen in ammonia ←-- NH_3 by the negative affinity of the copper in the two salts. But since the copper atom alone cannot combine directly with ammonia, it evidently does not possess negative affinity. Cuprous salts, however, can combine with ammonia, and cupric salts with a still larger quantity; hence the copper atom, on losing an electron, develops negative affinity, and with a loss of two the negative affinity becomes more marked. It therefore follows that the negative affinity of the copper is a secondary phenomenon which only appears when the primary affinity has come into action.

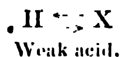
In this way the relative stability of the metalammine salts, as determined by Ephraim[1] from the temperature required to produce a constant dissociation pressure, can be readily explained.

Similar views have been applied to acids and bases. The strongest and weakest acids may be written :



---> H —> X --->

Strong acid.



H ←--> X

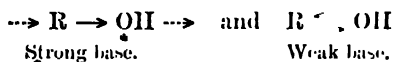
Weak acid.

If the secondary affinity of X in a weak acid is saturated by combination with a molecule M to give a complex acid, this complex acid will have the formula



---> H --> XM

and since the secondary affinity of X is now saturated, the secondary affinity of the hydrogen will be free, and its tendency to undergo electrolytic dissociation thereby increased. Whereas hydrocyanic acid is a very weak acid, hydrogen ferrocyanide, ferricyanide, and cobalticyanide are all strong acids. The same principles hold in the case of bases, the formulae for which fall between the types



---> R —> OH ---> and R ←--> OH

Strong base. Weak base.

When the secondary affinity of R in the weak base is saturated by combination with a molecule A, a complex and strong base of the formula (RA) —> OH is obtained, examples of which are afforded by the strongly alkaline compounds of ammonia with weakly basic metallic hydroxides. Moreover, two or more molecules of the same compound may be united by secondary affinity and give rise to polymerisation.

But there is a fundamental difference between secondary negative affinity and secondary positive affinity. According to the modern

[1] *Ber.*, 1912, 45, 1322; 1913, 46, 3103; 1914, 47, 1828.

view of the electrical structure of the atom, the positive nucleus is situated at the centre of the atom and its spatial dimensions are small compared with the volume of the whole atom. Secondary negative affinity depends on the power of the nucleus to attract lines of force (or electrons). Since the nucleus is so small and acts at the centre, it follows that the secondary negative affinity may be regarded as a force distributed over the surface of the atomic sphere. Secondary positive affinity, on the other hand, emanates from the outer, mobile, or valency electrons, and therefore is confined to individual electrons. It follows that when the atomic volume is large the unsaturated secondary affinity of the atoms in an electrolyte is large (though its intensity over a given area is small), thereby bringing about dissociation. This is why the salts of the alkali metals are strong electrolytes. The conception of secondary affinity leads, moreover, to the following conclusions. In compounds of the formula ABx, in which B represents a univalent atom and x varies from 1 to 8, when $x = 1$ the secondary affinity of A is only partly saturated because only a part of its spherical surface comes under the influence of B. With increasing value of x more of this surface is brought into action, and the tendency to dissociation, as is well known, falls away with increasing valency. In a non-polar compound secondary affinity must be completely saturated, and must occur when the atoms of B are symmetrically distributed, that is, when x is 4, 6, and 8. Such substances should not only be non-polar, but inert and volatile. It is, therefore, interesting to find that the gases methane, sulphur hexafluoride, tungsten hexafluoride, and the liquids carbon tetrachloride and the very volatile solids osmium octafluoride, osmium tetroxide, and ruthenium tetroxide, possess these properties.[1]

An interesting theory of the electronic structure of the atom, which determines its valency and other properties, has recently been put forward by Lewis and extended by Langmuir.[2]

REFERENCES.

The Theory of Valency, by J. N. Friend. Second edition. Text-books of Physical Chemistry. Longmans, 1915.

Outlines of Chemistry, Chapter IX, by H. J. H. Fenton. Cambridge Univ. Press, 1910.

Neuere Anschauungen auf dem Gebiete der anorganischen Chemie, 2nd ed. by A. Werner. Vieweg, Brunswick, 1909; or *New Ideas of Inorganic Chemistry*, by the same, translated by E. P. Hedley. Longmans, 1911.

Modern Electrical Theory, by N. R. Campbell. Cambridge Univ. Press, 2nd edition, 1913.

The Atomic Theory, by Sir J. J. Thomson. Clarendon Press, Oxford, 1914.

[1] *Trans. Chem. Soc.*, 1919, 115, 278.
[2] *J. Amer. Chem. Soc.*, 1916, 38, 762; 1919, 41, 868, 1543; 1920, 42, 274.

CHAPTER III

THE NATURE OF ORGANIC REACTIONS

In the preceding chapter we have discussed the valency of carbon and the views which have been put forward to explain the phenomenon. We have now to inquire into the causes which bring about the interaction of two substances.

Valency and Affinity. The first question which naturally suggests itself is what relation exists between valency and chemical affinity; does the quadrivalency of carbon, compared, say, with the univalency of chlorine, imply a correspondingly higher chemical affinity? Before answering this question it may be well to consider briefly the nature of chemical affinity, or the force which binds the elements together. This has already been touched upon in the previous chapter. It is generally assumed that opposite electrical properties of the elements determine the readiness with which they unite and the stability of the union. It is manifested by the evolution of heat or by the loss of some other form of energy. Thus, hydrogen and chlorine, representing a highly electropositive and electronegative element in the electrochemical series, unite with loss of energy, and this energy must be supplied if it is desired to break down the union; in other words, the greater the loss of energy, the greater the stability of the product. The compound formed in this case, namely, hydrogen chloride, is highly ionised in aqueous solution. Exactly the same is true of the compound of sodium and chlorine. On the other hand, we have the phenomenon of atoms of the elementary gases joining together in the form of molecules and of still more highly polymerised forms, as, for example, carbon and sulphur, of such stability that they are only decomposed with difficulty.

It is clear then that chemical affinity is at times independent of opposite electrical character unless we are prepared to admit, like Abegg and Bodländer and others (p. 101), that the atoms are furnished with both positive and negative charges which may be brought into

action when required. This view is, however, attended by serious difficulties, which may be illustrated in the case of carbon.[1]

Carbon, as already pointed out, occupies a unique position in the periodic table. Its position midway in the electrochemical series gives it a neutral character which enables it to enter into union with both electropositive elements, such as hydrogen, and electronegative elements like chlorine. It is noteworthy that although free carbon can only be induced to combine with great difficulty with either hydrogen or chlorine, the compounds formed, CH_4 and CCl_4, are not only stable at moderately high temperatures and under the action of many reagents, but are not appreciably dissociated in solution. Moreover, the elements linked to carbon retain something of their properties in the free state. Carbon, for instance, when combined with hydrogen, forms a strongly electropositive methyl group, but when joined to chlorine produces a strongly electronegative CCl_3 group. The effect is seen on introducing the two groups in place of hydrogen into formic acid. Acetic acid, $CH_3.COOH$, is weaker by about one-twelfth than formic acid, as proved by its affinity constant; trichloracetic acid has more than 5,000 times the strength.

This peculiar character of carbon of acting as a neutral atom to which other atoms may become attached without renouncing their original properties has been referred to by van 't Hoff[2] as *inertia* (Trägheit) and by Michael as *plasticity*.[3] It is to this same inert character that van 't Hoff attributes the slow reactivity of organic as compared with inorganic compounds, or, as we should now say, the smaller tendency to ionisation.[4]

But if carbon exerts little influence on the character of the atoms attached to it, it preserves the property, which it possesses in the free state, of polymerising, that is, of combining with itself to form aggregates of atoms and carbon chains. This again appears to be a peculiarity of its position in the periodic system; for the tendency to polymerise or to form chains falls away in the periodic groups lying to the right and left of carbon. Chains of three and four atoms of nitrogen are known, but are unstable, and attempts to lengthen them have met with increasing difficulty, whilst in the case of

[1] Some of the ideas which are expressed here are derived from the *Ansichten über die organische Chemie*, by J. H. van 't Hoff, 2 vols., 1878 and 1881, Vieweg, Brunswick. Although this classic is now nearly a third of a century old and appeared at a time when organic chemistry was undergoing its most rapid development, many of the views which find expression there are still eminently suggestive and as applicable to present-day problems as when they first appeared.

[2] *Ansichten*, vol. i, p. 214.

[3] *J. prakt. Chem.*, 1899, 60, 325.

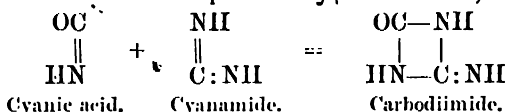
[4] *Ansichten*, vol. i, p. 286.

oxygen the peroxides, peracids, and ozonides readily and sometimes explosively break up and lose oxygen.

We may then ask: is this tendency to polymerise which is exhibited by free carbon in carbon chains effected by means of the opposite electrical polarities of the individual atoms? If so, the end atoms of a chain, like the top and bottom discs of a voltaic pile, should show opposite polarities; but there is no evidence that this is the case. For if it were so, the halogen atoms at the two ends of a carbon chain should possess different reactivities, which they do not, otherwise hexylene dibromide and sodium should yield dodecylene dibromide, $C_{12}H_{24}Br_2$, whereas cyclohexane is formed.[1]

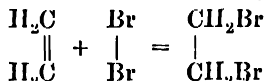
We may therefore conclude that the tendency to polymerise, like chemical affinity, is a function of the atomic weight and is associated with the position of the element in the periodic system; that increase of valency up to the central group is not attended by an increase, but by a decrease in chemical energy.[2] According to van 't Hoff[3] it is the high valency combined with the chemical inertia of carbon which determines its union with so many different elements, as well as with itself, and which explains at the same time the formation of the vast number of organic compounds.

Types of Reactions. What, then, determines chemical union? Before answering this question we will consider the different kinds of organic reactions. Van 't Hoff[4] classifies them into three types. In the first, addition occurs between two unsaturated molecules by means of one of the double bonds without cleavage of either molecule. The product has in consequence a cyclic structure,



Cyanic acid. Cyanamide. Carbodiimide.

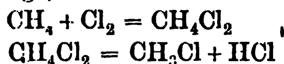
In the second type, addition occurs between an unsaturated and a saturated molecule, with cleavage of the saturated molecule. The additive compounds, which the olefines form, come under this head.



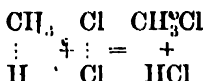
The third type represents ordinary substitution in which both molecules are saturated.[5]

[1] W. H. Perkin, *Ber.*, 1894, 27, 216.
[2] Blomstrand, *Chemie der Jetztzeit*, 1869, 217, 213. Hinrichsen, *Zeit. physik. Chem.*, 1901, 39, 305.
[3] *Ansichten*, vol. ii, p. 240. [4] *Ansichten*, vol. i, p. 8.
[5] There is a fourth type in which the molecule interacts with itself, condenses

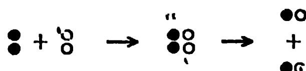
To explain the union of methane with chlorine we shall have to assume one of two things, either that addition precedes substitution,



or that each molecule under the influence of the other dissociates, the methane into methyl and hydrogen, and molecular into atomic chlorine.



The first view was held by A. Kekulé, and in a modified form by J. U. Nef; the second by Williamson, who gave expression to it in propounding his 'Theory of Etherification' (1851). Kekulé, in his *Lehrbuch* (1867), says: 'When two molecules react upon one another, they attract one another by their affinity and unite; the relation between the affinities of the single atoms frequently causes the atoms, which had previously belonged to different molecules, to come into the closest attachment. On this account the atomic groups which were originally separated in one direction, when joined to the other molecule, separate in another direction.' The process may be represented by black and white spheres, thus:



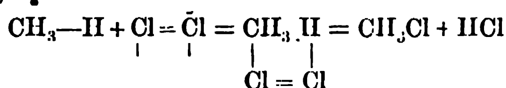
This view has been very generally adopted. Van 't Hoff[1] has pointed out that many substitution processes may be most simply explained by addition, and Michael[2] has accepted the same view, which will be more fully discussed later. It receives further support from the theory of enzyme action, according to which enzyme and substrate unite before cleavage (Part III, p. 98), and from Fischer's explanation[3] of optical inversion (Part II, p. 197), whereby the reagent, which causes it, is represented as attaching itself to the atom before forming an additive compound which subsequently breaks down in a manner which may or may not cause a change in the spatial arrangement of the remaining groups. The researches of Schmidlin and Lang,[4] who have been able to prove the existence of such additive compounds from a study of the melting-point curves of reacting compounds, point in the same direction. The theory also

or polymerises. All the four types may occur in the case of a single compound as illustrated by the ketones (p. 66).

[1] *Ansichten*, vol. i, pp. 225, 214.
[2] *J. prakt. Chem.*, 1883, 37, 486.
[3] *Annalen*, 1911, 381, 123.
[4] *Ber.*, 1910, 43, 2806; 1912, 45, 899.

fits in with Werner's notion of residual affinity or auxiliary valencies. In this connection it is interesting to note that Kekulé, who was a strong supporter of the theory of fixed valency, should have originated an idea which was directly opposed to it.

Nef[1] considers that chemical reactivity depends on dissociation, and at the same time on the additive power of the substituting molecule, by virtue of its residual valencies.



Both these views have been extended to the synthesis of organic compounds, in which wide scope is given to their application (p. 280).

There is a fourth type of reaction in which both reacting molecules are saturated, yet unite without cleavage. Under this type may be included those loose combinations, commonly known as molecular compounds, represented by substances containing alcohol, benzene, and chloroform of crystallisation, those formed by the union of aromatic nitro and nitroso compounds[2] with aromatic hydrocarbons and amino compounds, perbromides of the organic bases, and compounds such as piperidine and carbon tetrabromide, $C_5H_{11}N(CBr_4)$.[3] As already stated, such combinations find no place in the ordinary views of a definite valency number, but are readily explained on Werner's theory.

Among the many reactions, drawn from one or other of the different types, which might be discussed, we propose to limit ourselves for the present to those of the unsaturated compounds, as having been most carefully studied and affording the most varied and most interesting results.

Addition. Reactions of Unsaturated Compounds. The simplest case of a reaction between molecules is one where direct union occurs. The theory of unsaturated compounds depends in the first instance on the formation of what are termed additive compounds (p. 113). Where they are formed it is possible, as a rule, to discover one or more elementary atoms in the original compound whose maximum valency has not been utilized, and these atoms are represented as points of attachment for the new molecule or molecules. Thus, hydrocarbons of the ethylene and acetylene type and their derivatives,

[1] *Annalen*, 1891, **266**, 59; *Journ. Amer. Chem. Soc.*, 1904, **26**, 1563.
[2] Schraube, *Ber.*, 1875, **8**, 617.
[3] Dehn and Dewey, *Journ. Amer. Chem. Soc.*, 1911, **33**, 1588.

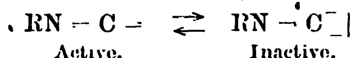
also aldehydes and ketones, cyanides and isocyanides, cyanates and isocyanates, azo- and diazo-compounds, &c., all of which form additive compounds, are readily explained on the theory of the unsaturation of certain atoms.

But there are numerous other compounds which form simple additive compounds where the explanation is not so simple. In the pyrones[1] the oxygen is made quadrivalent in order to afford a convenient point of attachment for the molecule of acid with which they unite, and the structure of the quinhydrones (Part II, p. 120) is explained in the same way. The existence of molecular compounds of aromatic hydrocarbons, phenols, and amino-compounds with di- and tri-nitrobenzene and picric acid, and of the perbromides of bases, &c., affords further examples for which unsaturation cannot conveniently be made to serve. It is for this reason, as we have seen, that Werner has introduced the notion of auxiliary in addition to ordinary or principal valencies (see p. 90).

Nor is it every unsaturated compound that is capable of forming an additive compound; there are, for example, hydrocarbons of the ethylene type which refuse to unite with hydrogen, halogen acid, or halogen. We are thus confronted with conditions in which, on the one hand, atomic unsaturation is for some reason suspended, and in which, on the other hand, addition occurs where unsaturation cannot be assumed.

A study of the conditions determining unsaturation may throw some light on the nature of this property.

Nef[2] divides unsaturated compounds into three categories, namely, those which contain a single, active, unsaturated carbon atom, such as carbon monoxide, the alkyl and acyl isocyanides, hydrocyanic acid, fulminic acid and its salts, and mono- and di-halogen substituted acetylenes. They exhibit unsaturation in the same way as compounds of the second or ethenoid type, with the difference that the new pair of atoms or groups attach themselves to the same carbon atom instead of distributing themselves between two. The bonds may be free and active, or latent and inert, but it is only in the former condition, according to Nef, that addition can occur. The two are in dynamic equilibrium, and may be represented in the case of the alkyl isocyanides in the following manner:



The process of addition is supposed to occur by partial or complete

[1] *Trans. Chem. Soc.*, 1899, 75, 710. [2] *Journ. Amer. Chem. Soc.*, 1904, 26, 1549.

dissociation of the addendum into its atoms or constituent groups, which then unite with the active valencies of bivalent carbon. Thus the isocyanides form additive compounds with chlorine in the following way:



The other additive compounds of the isocyanides have already been discussed under bivalent carbon (p 65). The second class of unsaturated compounds includes those of the ethylene type which combine by direct addition to a pair of unsaturated atoms, and constitutes the largest and most important class.

The third group includes those closed atomic chains such as cyclopropane and propylene oxide, which, though apparently saturated, unite with halogens, halogen acids, &c., like the olefines (p. 180).

Addition (Ethenoid Compounds). Ethenoid compounds, it is well known, enter as a rule into union with hydroxyl, ozone, the halogens, halogen acids, sulphuric and hypochlorous acid, nitrosyl chlorides, nitrogen tri- and tetroxide, and less frequently with ammonia, the amines, mercaptans, and alcohols.[1] The subject has been carefully studied by Michael,[2] who has laid down certain general propositions, which he regards as determining the course of these and similar reactions. Adopting the principle proposed by Ostwald that 'every system tends towards that state whereby the maximum entropy is reached', Michael[3] replaces the word entropy by *chemical neutralisation*, that is, the neutralisation of the chemical energies or affinities of the reacting atoms. He has further applied Ostwald's idea of the distribution of affinity among acids, or *avidity*,[4] to the formation of additive compounds under the term *distribution principle*, which he explains as follows:

'If two unsaturated atoms *A* and *B* are present in an organic molecule which exhibit unequal affinity towards *C* and *D* of the addendum *CD*, and if *A* has a greater affinity for *C* than *B* has, addition will occur if the affinity of $AC+BD$ is greater than that of *CD*, and the more readily and completely the larger the difference. In this process of addition not only the affinity of *A* to *C* and of *B* to *D* comes into action, but also that of *A* to *D* and of *B* to *C*, and therefore the further possibility is presented, not only of the combination of $AC+BD$, but of $AD+BC$, and the latter in increasing

[1] For a more complete list see J. U. Nef, *Annalen*, 1897, 298, 206.
[2] *J. prakt. Chem.*, 1899, 60, 286, 410; *Ber.*, 1906, 39, 2138.
[3] *J. prakt. Chem.*, 1899, 60, 292.
[4] Thomsen, *Pogg. Ann.*, 1869, 135, 497.

proportion the nearer the two combinations $AC+BD \rangle AD+BC$ approach one another. If the relations are changed in any way so that the affinity of A to C exceeds relatively that of B to C, the formation of $AC+BD$ must increase at the expense of $AD+BC$, and if B has a greater affinity than A to D it may happen that the amount of $AD+BC$ becomes so small as practically to vanish.'

This principle, taken in conjunction with that of maximum neutralisation, will determine the course of the additive process. The latter may take the form of what is termed by Michaël the *negative-positive rule*, where the maximum neutralisation is attained by the electronegative atom or group of the addendum attaching itself to the more electropositive atom of the unsaturated molecule, and the more electropositive atom to the more electronegative part of the molecule.[1] For example, in propylene, $CH_3.CH:CH_2$, the electropositive radical CH_3 will influence the central more than the end ethenoid carbon by rendering it more electropositive. Consequently, on the addition of hydrogen iodide, the electronegative iodine atom will be mainly attracted to the central carbon. This proves to be the case. At the same time a small amount of normal propyl iodide is formed in agreement with the principle of distribution.

If in place of hydrogen iodide, whose constituents lie widely apart in the electrochemical series, ICl be added to the compound, a certain quantity of $CH_3.CHI.CH_2Cl$ should be formed in addition to $CH_3.CHCl.CH_2I$. If, again, BrCl be employed, the relative quantities of the two products must become still more nearly equal. Experiment has fully confirmed this result, for Michael found that the proportion of primary to secondary chloride in the first case was 1 : 3, and in the second 5 : 7.[2]

The action of negative groups in the unsaturated compound will also influence the result by rendering the neighbouring ethenoid carbon more negative. This is a common observation among unsaturated acids, like acrylic acid, with a strongly negative carboxyl group. Here the halogen of the halogen acid attaches itself to the β carbon.

From the above considerations, the rule laid down by Markownikoff[3] that the halogen of a halogen acid attaches itself to the least hydrogenated carbon, though by no means free from exceptions, will be readily understood; for the least hydrogenated carbon will usually be the one situated next to the strongest electropositive hydrocarbon

[1] *J. prakt. Chem.*, 1892, 46, 205. [2] *J. prakt. Chem.*, 1892, 46, 315, 452.
[3] *Annalen*, 1870, 153. 256.

radical. Let us take the case of a substituted olefine such as β-bromopropylene, $CH_3 . CBr : CH_2$. The addition of hydrogen bromide produces $\beta\beta$-dibromopropane.[1] The effect here is due, according to Michael, to the neutral character of the carbon atom, whereby the mutual attraction of the bromine atoms in the free state is still exerted, under the concurrent influence of the electro-positive methyl group. If, on the other hand, the bromine occupies the α position, $CH_3 . CH : CHBr$, the attraction of the bromine atom as well as the proximity of the methyl group act in opposition; the hydrogen bromide distributes itself, so that both propylene bromides are formed, namely, $CH_3 . CHBr . CH_2Br$, $CH_3 . CH_2 . CHBr_2$.

Michael[2] considers that in longer chains reactivity may be influenced and modified by spatial considerations, and that, for example, a carbon group in position 5 and 6 relatively to the unsaturated carbon atom may, by its tendency towards ring-formation, and, therefore, by its proximity to the unsaturated carbon atoms, determine the character of the product. In this way either the direct or indirect influence of each atom will be exerted according to its position, and determine the course of the reaction,[3] that of the atoms in direct connection with the reacting group naturally predominating.

Much the same conditions as those which determine addition should affect the removal of halogen acids by alkalis, and some of the experimental results will now be briefly referred to.

In propylene bromide, for example, the effect of the positive methyl group will not only be distributed between the two other carbon atoms, but will be directed in a greater degree towards the retention of the bromine atom in the β position. It has been found that the proportion of $CH_3 . CBr : CH_2$ to $CH_3 . CH : CHBr$ is two to one. As β-bromopropionic acid is more readily formed from acrylic acid than the α compound, the former loses hydrogen bromide more readily. Isobutylene yields tertiary butyl bromide, and it is found that the latter, of all the isomers, is most readily converted into isobutylene.

Similarly with the dihalogen compounds; the more readily bromine is added, the more easily is it, as a rule, removed. Generally speaking, the hydrogen of the least hydrogenated carbon is detached;[4] but its removal depends upon the proximity of methyl groups, which by increasing the positivity of the carbon diminishes

[1] Reboul, *Ann. Chim. Phys.*, 1878, 14, 465.
[2] *J. prakt. Chem.*, 1892, 46, 335.
[3] See van 't Hoff's *Ansichten*, vol. i, p. 284, vol. ii, p. 252
[4] Saytzeff, *Annalen*, 1875, 179, 280.

its affinity for hydrogen. $(CH_3)_2CH.CHBr.CH_3$ gives mainly trimethylethylene $(CH_3)_2.C:CH.CH_3$, and a little isopropylethylene $(CH_3)_2CH.CH:CH_2$.

The little that has been systematically investigated on the addition of hypochlorous acid, ammonia, and alcohol is referred to by Michael.[1]

In the above examples we have considered mainly the nature of the addenda. We will now extend the inquiry into the effect on addition of introducing other groups into the ethenoid molecule in place of hydrogen. A considerable amount of work has been done on this subject by Klages, Bauer, and Nef.

Addition of Hydrogen. Klages[2] has studied the reduction of two series of ethylene derivatives, in one of which a hydrogen atom is replaced by phenyl, and in the other by carboxyl. Other hydrogen atoms are replaced by methyl, benzyl, and phenyl groups. The reduction appears to be inhibited where two methyl groups replace both the hydrogen atoms attached to the same carbon atom; in other words, by augmenting the positive character of the carbon group affinity for hydrogen is diminished. Thus, dimethyl and ethyldimethyl styrene $C_6H_5CH:C(CH_3)_2$, $C_6H_5C(C_2H_5):C(CH_3)_2$, β-dimethylacrylic acid $COOH.CH:C(CH_3)_2$, and teraconic acid $COOH.C(CH_2COOH):C(CH_3)_2$, are either reduced with great difficulty or not at all. The same applies to terpinolene (Part III, p. 257) and to methylheptenone (Part III, p. 257), both of which contain the group $C:C(CH_3)_2$.

Addition of Bromine. Bauer[3] has examined the effect of substituents on the additive power of ethenoid compounds for bromine. His results are formulated in the following statement: 'the tendency of a carbon double bond to add bromine is diminished if in the case of both carbon atoms reduplication of carboxyl, ester, phenyl groups, or bromine has taken place.' Here the accumulation of negative groups affects the addition of negative atoms. In the acrylic acid series, the substitution of hydrogen by one or more methyl groups or one bromine atom attached to either carbon does not prevent addition; but neither tribromacrylic nor dibromocrotonic acid combine. Further, dimethylfumaric acid (pyrocinchonic acid), diethylfumaric acid (xeronic acid), dibromo- and methylbromo-fumaric acid, acetylene tetracarboxylic and α-phenylcinnamic acid do not lend themselves to addition of bromine,

[1] *J. prakt. Chem.*, 1899, 60, 431, 463, 467. [2] *Ber.*, 1904, 37, 924, 1721, 2301. [3] *Ber.*, 1904, 37, 3317.

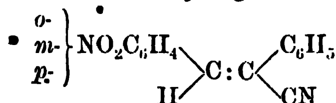
whereas both maleic and fumaric, methylfumaric and bromomaleic acids combine. Here the multiplication of both positive and negative groups prevents addition, a fact which steric hindrance may possibly serve to explain.

Sudborough and Thomas[1] have shown that the unsaturation of $\beta\gamma$ unsaturated acids is much greater than that of $\alpha\beta$ acids, and the rapid addition of bromine in the former case serves as a method for distinguishing the two classes. The difference in the case of the $\alpha\beta$ acids is attributed to conjugation, which is explained on p. 133.

The addition of halogens is also modified by light, and will be referred to in the section on photochemistry (Part II, p. 141).

It is an interesting fact, that whereas cinnamic acid and crotonic acid do not unite with iodine, phenylpropiolic acid and tetrolic acid, $CH_3C:C.COOH$, combine with two atoms of the element.

Turning to the hydrocarbons, stilbene $C_6H_5CH:CH.C_6H_5$ and its monomethyl and monobromo derivative add bromine, but not the dibromo derivative. Where both phenyl groups are attached to the same carbon atoms as in diphenylethylene $(C_6H_5)_2C:CH_2$ and its mono- and di-methyl derivatives, bromine addition takes place, but is prevented in $(C_6H_5)_2C:C(C_6H_5)_2$, $(C_6H_5)_2C:CHBr$, and $(C_6H_5)_2C:CBrCH_3$, that is, where two phenyl groups or bromine are attached to the second ethenoid carbon. The presence of chlorine and cyanogen produce the same effect as bromine.[2] A further fact of interest mentioned by Bauer is that phenylcinnamic nitrile adds bromine, forming a definite bromide, but a nitro group in the para position prevents the addition. The *m*-nitro compound, on the other hand, yields a definite additive compound, whilst the *o*-nitro compound occupies a middle position, bromine being partially decolorised without evolution of hydrogen bromide.



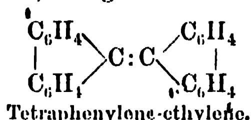
Nitrophenylcinnamic nitrile.

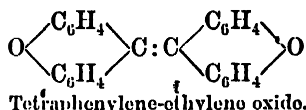
The retarding effect of phenyl, carboxyl, and cyanogen follow in increasing order, $C_6H_5 < COOH < CN$, which agrees with the affinity constants of the acids in which they occur :

		K
Phenylacetic acid	$C_6H_5.CH_2.COOH$	0·00556
Malonic acid	$COOH.CH_2.COOH$	0·045
Cyanacetic acid	$CN.CH_2.COOH$	0·37

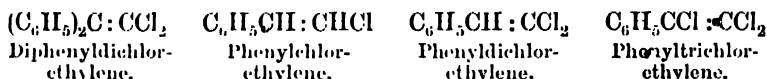
[1] *Trans. Chem. Soc.*, 1910, 97, 715. [2] Bauer, *J. prakt. Chem.*, 1905, 72, 201.

The results of these observations appear to fall in with Michael's neutralisation or positive-negative rule; for the addition of positive hydrogen atoms is retarded by reduplication of positive radicals in the ethenoid molecule, and negative bromine atoms by the presence of negative radicals. On the other hand, Biltz[1] has pointed out that, although tetraphenylethylene does not unite with bromine, the closely allied compounds tetraphenylene-ethylene and its oxide combine, though in the second case with difficulty.


Tetraphenylene-ethylene.


Tetraphenylene-ethylene oxide.

Also, diphenyldichlorethylene, phenylmono-, di-, and tri-chlorethylene, as well as tetrachlorethylene in sunlight, form additive compounds in spite of the multiplication of negative groups.



$(C_6H_5)_2C:CCl_2$	$C_6H_5CH:CHCl$	$C_6H_5CH:CCl_2$	$C_6H_5CCl:CCl_2$
Diphenyldichlorethylene.	Phenylchlorethylene.	Phenyldichlorethylene.	Phenyltrichlorethylene.

But addition is inhibited in the case of diphenyldinitroethylene, $C_6H_5C(NO_2):C(NO_2)C_6H_5$.

The evidence is very conflicting. Bauer[2] adopts Hinrichsen's view that negative groups in sufficient number and strength weaken the fourth valency of carbon, just as phosphorous pentachloride overloaded with negative atoms loses chlorine on heating, and passes to a state of lower and more stable valency. The valency of carbon, in the same way, when overloaded with negative atoms or groups, tends to shrink and become tervalent. From this point of view there is nothing remarkable in the existence of triphenylmethyl (p. 60).

Exactly similar views have been expressed by Michael[3] on the instability of carbon compounds when charged with either negative or positive atoms or groups. Methane is a stable neutral compound because the negative carbon is neutralised by the four positive hydrogen atoms; but if hydrogen is replaced by an electropositive metal, as in the organo-metallic compounds, there is a surplus of positive polarity, and a consequent loss of stability. The combined loss of stability and active valency is, no doubt, a gradual one, and varies in different compounds, so that the addition or removal of bromine is probably a reversible process, the balance of which may shift from one side, where no addition occurs under any circum-

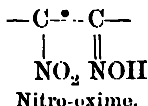
[1] *Annalen*, 1897, **296**, 231, 263. [2] *Annalen*, 1904, **336**, 223.
[3] *J. prakt. Chem.*, 1899, **60**, 302.

stances, to the other, where the ethylene compound is wholly converted into a definite and stable bromide.

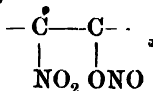
Addition of Nitrosyl Chloride. The union of nitrosyl chloride with unsaturated compounds was first studied by Tilden,[1] who found that addition occurs in the case of limonene, pinene, trimethyl-, tetramethyl-, and methylpropyl-ethylene, normal octylene, phenylethylene (cinnamene), and diphenylethylene, oleic and elaidic acids, anethole and isosafrole; but not with acenaphthylene, eugenol, safrole, *w*-nitrocinnamene, crotonic, isocrotonic, fumaric, and maleic acids. There appears to be no relation between the additive power for nitrosyl chloride and that for bromine.

Addition of Nitrogen Trioxide. The property of forming additive compounds with N_2O_3 is also found among the terpenes. The nature of the product may vary according to the environment, giving rise to nitroso-nitro compounds or nitro-oximes.[2]

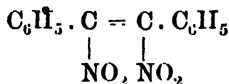

Nitroso-nitro.


Nitro-oxime.

Addition of Nitrogen Tetroxide. Many of the terpenes and unsaturated ketones[3] are known to form additive compounds with nitrogen tetroxide, forming nitrosates containing the group,



which, in the case of unsaturated ketones, readily loses HNO_2, and passes into unsaturated nitro compounds. Schmidt[4] has shown that with diphenylacetylene both cis and trans stereoisomers of dinitrodiphenylethylene are formed,

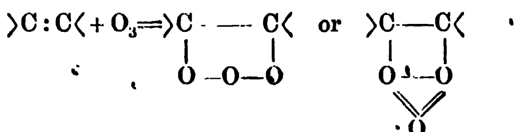


and Biltz[5] has found that this property is shared by tetrachlor- and tetrabrom-ethylene. In the case of the tetraiodo compound, substitution of the iodine occurs.

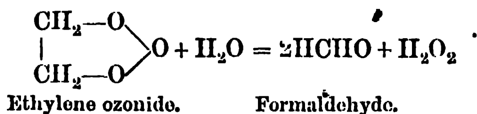
Addition of Hydroxyl and Ozone. A characteristic property of the ethenoid carbon atom is its power of taking up two hydroxyl

[1] *Trans. Chem. Soc.*, 1894, 1, 324.
[2] Wieland, *Annalen*, 1903, 328. 154; 1903, 329, 225; 1905, 340, 63.
[3] Wieland and Bloch, *Annalen*, 1905, 340, 163.
[4] *Ber.*, 1901, 34, 619.
[5] *Ber.*, 1902, 35, 1528.

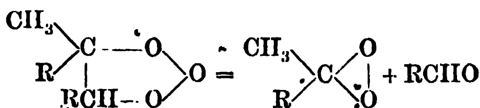
groups when oxidised by a dilute and neutral solution of permanganate, usually at the ordinary temperature. This reaction has been utilized in ascertaining the position of a double link as well as in effecting the cleavage of the molecule by further oxidation at this point: $>C = C< + H_2O + O = >C(OH)-C(OH)<$. Many examples of this reaction will be discussed in later chapters. Another property which appears to be shared by acetylene compounds is the union of ethenoid compounds with one molecule of ozone, forming a class of compounds known as *ozonides*.



The formation and properties of these compounds have been exhaustively studied by Harries and his co-workers.[1] They are obtained by passing ozonised oxygen (containing about five per cent. of ozone) into a solution of the unsaturated compound in an inert solvent along with a current of carbon dioxide, which diminishes the risk of explosion, some ozonides being extremely explosive. They are thick colourless oils, syrups, or gelatinous masses, which liberate iodine from potassium iodide and bleach permanganate and indigo. They have a peculiarly unpleasant and suffocating smell, and some, such as the ozonides of mesityl oxide and acrolein, are explosive, but not those of the unsaturated hydrocarbons, the simpler members of which are sufficiently stable to be distilled in vacuo. With water they decompose at the original double bond into aldehyde or ketone and hydrogen peroxide.



In other cases, where excess of ozone is used, the ozonide breaks up and gives the peroxide of the one carbon group and the aldehyde or ketone of the other.

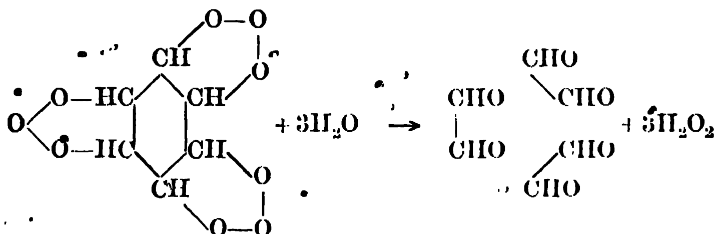


The formation of ozonides may be used for determining the presence and, frequently, the position of a double bond, and the

[1] *Annalen*, 1905, 343, 311; 1915, 410, 1.

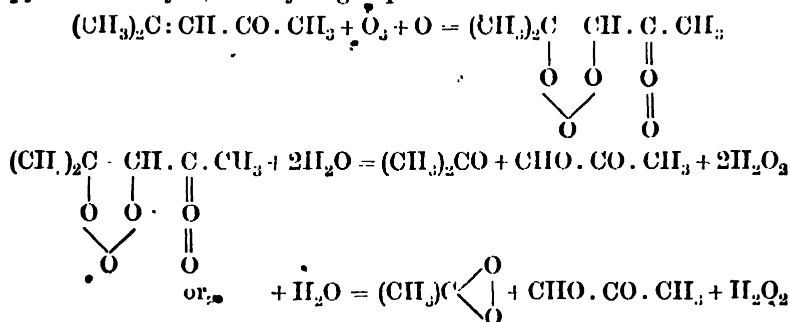
process has been applied in the case of pulegone, pinene, and other compounds.

The fact that benzene forms a triozonide may therefore be taken as evidence of the Kekulé formula. This compound breaks up with water like other ozonides, giving three molecules of glyoxal.



Naphthalene, however, only unites with two molecules of ozone, both of which are attached to the same nucleus, and consequently, according to Harries, the two nuclei are differently constituted.

The action of ozone on aldehyde and ketone groups is to furnish one additional atom of oxygen, and form a peroxide, so that a substance like mesityl oxide, which contains a ketone group in addition to an ethylene linkage, unites with four atoms of oxygen, the product breaking up with water into acetone (or acetone peroxide), pyruvic aldehyde, and hydrogen peroxide:



Autoxidation. The behaviour of unsaturated compounds towards ozone leads directly to the action upon them of free oxygen, and to the explanation of the phenomenon known as autoxidation, which was first studied by Schönbein. The property which turpentine oil possesses when exposed to air of absorbing oxygen, which is thereby rendered active and capable of bleaching indigo, separating iodine from potassium iodide, oxidising arsenious to arsenic acid, &c., has long been known, and the induced activity has been variously ascribed to the formation of ozone, hydrogen peroxide, and atomic

oxygen. A different interpretation of the process has been offered by Moritz Traube and Engler and Weissberg[1] on the following grounds: turpentine oil will retain its oxidising properties for years in the dark in absence of air, a condition which would scarcely obtain if ozone or atomic oxygen were in contact with so oxidisable a substance as turpentine. The oxygen which turpentine absorbs is not displaced by passing inert gases through the liquid, indicating some form of combination. The activity cannot be due to dissolved hydrogen peroxide, since the latter cannot be removed by shaking with water, whereas from an artificially prepared mixture it is completely extracted. Moreover, oxidised turpentine oil, unlike hydrogen peroxide, separates iodine from potassium iodide in absence of an acid, and gives no blue colour with chromic acid solution and other such as a trace of hydrogen peroxide will produce. On the other hand, the oxidised turpentine gives the yellow colour with titanic acid, characteristic of all peroxides. The conclusion arrived at by the authors is that the oxygen attaches itself in the molecular form to the substance, yielding a peroxide which may undergo intramolecular rearrangement into the ordinary atomic form, or may give up a portion of its oxygen to an oxidisable substance in its vicinity. In this way many substances which are not directly oxidisable by free oxygen can be oxidised indirectly by the peroxide. The authors of the theory term the peroxide or *moloxide* the *autoxidator*, the substance indirectly oxidised the *acceptor*, and formulate the process as follows:

$$\underset{\text{Autoxidator.}}{AO_2} + \underset{\text{Acceptor.}}{B} \longrightarrow AO + BO$$

A behaviour precisely similar to that of turpentine has been observed in the case of other unsaturated hydrocarbons, amylene, trimethylethylene, hexylene, fulvene and its derivatives (Part II, p. 92), &c., and may be represented as follows:

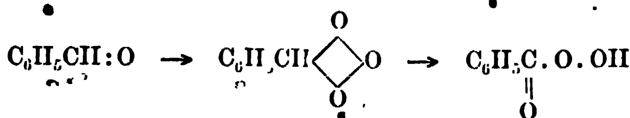
$$-C{=}C- + O_2 = \begin{array}{c}-C-C-\\ \;\;|\quad\;| \\ \;\;O-O\end{array}$$

in which molecular oxygen adds itself to the ethenoid carbon atoms after the manner of ozone.

The discovery by Baeyer and Villiger[2] of the existence of a definite though highly unstable peroxide of benzaldehyde has afforded strong evidence in favour of the above view. The substance

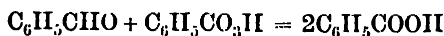
[1] *Vorgänge der Autoxydation.* Vieweg, Brunswick, 1904.
[2] *Ber.*, 1900, 33, 858, 1569.

was obtained by the action of hydrogen peroxide on benzaldehyde as a colourless crystalline compound having an acid character and forming salts. According to Engler and Weissberg it is produced by addition of molecular oxygen followed by intramolecular change.



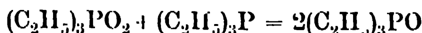
Benzoyl hydroperoxide.

Benzoyl hydroperoxide has similar properties to oxidised turpentine, inasmuch as it is not only capable of oxidising a second substance such as indigo, but can react upon itself and, by parting with an atom of oxygen to a second molecule of benzaldehyde, yield two molecules of benzoic acid:



$$C_6H_5CHO + C_6H_5CO_3H = 2C_6H_5COOH$$

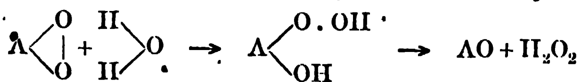
A similar process has been observed in the case of triethylphosphine, which, by absorption of oxygen, forms a peroxide, $(C_2H_5)_3PO_2$, capable of reacting on the unchanged substance, giving two molecules of monoxide:



$$(C_2H_5)_3PO_2 + (C_2H_5)_3P = 2(C_2H_5)_3PO$$

Many other examples of peroxide formation by absorption of free oxygen might be quoted, such as the conversion of phenylhydroxylamine into azoxybenzene,[1] and β-methylhydrindone into benzylmethylketone *o*-carboxylic acid,[2] but sufficient has been stated to illustrate the parallelism which exists in the behaviour of free oxygen and ozone.

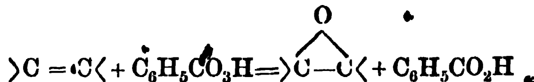
But in addition to the secondary processes above described, namely, the interaction of the peroxide compound with a foreign oxidisable substance, and also with itself, other secondary changes may and often do occur, such as the polymerisation of the peroxide, observed in the case of acetone peroxide, and the action of water on the peroxide, which may lead to the formation of hydrogen peroxide. The appearance of hydrogen peroxide when oxidised turpentine is left in contact with water has been explained in this way:



More recently, peroxides have been used for oxidising the ethenoid

[1] Bamberger, *Ber.*, 1894, 27, 1551.
[2] Kipping and Salway, *Trans. Chem. Soc.*, 1909, 95, 166.

group by delivering up an atom of oxygen. Ethylene oxides can be prepared in this way by the use of benzoyl hydroperoxide.

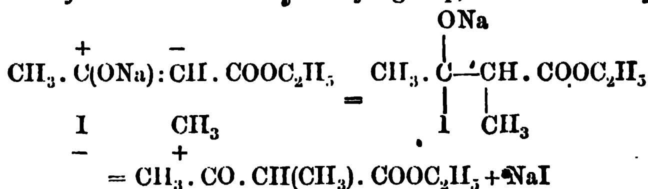


$$>C=C< + C_6H_5CO_3H = >C\overset{O}{-}C< + C_6H_5CO_2H$$

The application of other organic peracids to the oxidation of anhydrides has also been studied.[1]

Heterogeneous Addition. We have so far considered the nature of addition where the constituents of the addendum are similar, as in bromine, or dissimilar, as in hydrogen iodide, and again where the ethenoid carbon atoms are linked to different groups. There is a third case where both the ethenoid carbons are attached to different radicals, and the addendum consists of heterogeneous constituents. Examples of this type are considered on p. 203, and need not be referred to at length. The most interesting cases are perhaps those reactions in which the alkyl and acyl halide react with the metallic compounds of acetoacetic ester and Michael's reaction (p. 202). Here the electrochemical characters again appear to determine the course of the additive process, the positive and negative groups on both sides distributing themselves in such a way as to produce, according to Michael, the maximum neutralisation of affinities.

For example, the negative iodine atom of the alkyl iodide attaches itself to the carbon which is rendered positive by methyl and the ONa group, and the positive alkyl group to the negative carbon made negative by the associated carboxyl group, that is to say, the

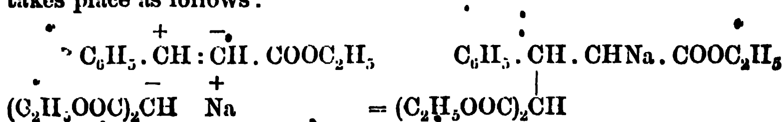


$$\overset{+}{CH_3 . C(ONa)} : \overset{-}{CH} . COOC_2H_5 \quad \underset{-}{I} \quad \underset{+}{CH_3} = CH_3 . C(ONa)(I)—CH(CH_3) . COOC_2H_5$$

$$= CH_3 . CO . CH(CH_3) . COOC_2H_5 + NaI$$

substitution is preceded by addition, an assumption which is by no means improbable.

In Michael's reaction similar conditions are supposed to prevail. The union of cinnamic ester and sodium malonic ester probably takes place as follows:



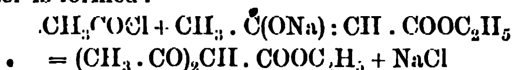
$$C_6H_5 . \overset{+}{CH} : \overset{-}{CH} . COOC_2H_5 \quad (C_2H_5OOC)_2\overset{-}{CH} \quad \overset{+}{Na} = C_6H_5 . CH(CH(COOC_2H_5)_2) . CHNa . COOC_2H_5$$

[1] *Amer. Chem. Journ.*, 1905, 32, 113.

An interesting question arises as to what would occur if in the first of these two reactions the metal were made less positive and the addendum more negative. What, in short, would happen if silver were substituted for sodium, and an acyl for an alkyl radical? The subject has been investigated by Michael.[1] He finds that if the relations of the two unsaturated atoms are so changed that their affinity to methyl is diminished more than that of the metal-oxygen, the tendency of the reaction will be towards substitution rather than addition. Silver acetoacetic ester and methyl iodide still give methyl-acetoacetic ester, but less readily and with decreased yield. If the negative chloroformic ester is substituted for methyl iodide, substitution occurs and not addition, and the acidic group attaches itself to oxygen.[2]

If, again, the ketone group is made more acidic, as, for example, in oxaloacetic ester, $C_2H_5OOC.CO.CH_2.COOC_2H_5$, the alkali compound furnishes only a poor yield of C-alkyl derivative, but an excellent yield of the O-alkyl compound, especially if the less positive silver salt is used.

The action on sodium acetoacetic ester of a strongly negative halide compound, such as acetyl chloride, is interesting, for its tendency to unite with oxygen is small in spite of the presence of the strongly electropositive alkali metal, and consequently diaceto-acetic ester is formed:



$$CH_3COCl + CH_3.C(ONa):CH.COOC_2H_5$$
$$= (CH_3.CO)_2CH.COOC_2H_5 + NaCl$$

It is not, however, clear from Michael's theory why the union between acetyl chloride and acetoacetic ester, in presence of so weak a base as pyridine, should give rise to acetoxycrotonic ester, $CH_3.CO(CO.CH_3):CH.COOC_2H_5$ rather than its isomer.

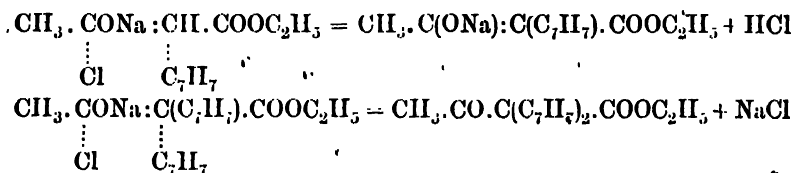
Nef[3] has expressed much the same view, namely, that the metal is attached to oxygen, and that alkyl and acyl halides may react by addition. He has shown that by the action of acetyl chloride on the sodium compound both products, namely, a little O-acetyl along

[1] *J. prakt. Chem.*, 1899, 60, 316; see also Lander, *Trans. Chem. Soc.*, 1900, 77, 729.

[2] This is in accordance with a more general law enunciated by Michael, whereby carbon, when attached to negative atoms or groups, shows less tendency to combine with itself (polymerise). Carbon monoxide can exist as a single molecule, but in union with metals polymerises, giving $(COK)_6$, $(CO)_6Ni$, $(CO)_6Fe$. On the other hand, the non-existence of methylene and methyl is due to the opposite tendency of the presence of electropositive atoms to cause polymerisation (*J. prakt. Chem.*, 1899, 60, 295).

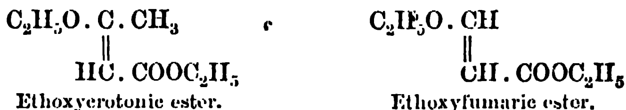
[3] *Annalen*, 1891, 266, 52; 1893, 276, 235; 1894, 280, 314.

with the C-acetyl derivative are formed. The main difference between these observers is that Nef regards both the free acetoacetic ester as well as its sodium derivative as possessing the hydroxyl formula, a view which has since been disproved. Moreover, he assumed that the halogen united with the α-hydrogen of the ester rather than with the sodium atom. He bases the latter view on the observation that benzyl chloride, and also acetyl and benzoyl chloride acting on the sodium compound, give both mono and dialkyl and acyl derivatives, which he expresses as follows:



It seems improbable that if sodium chloride were eliminated at the first stage the product, which contains a benzyl group and is therefore more positive, should decompose the sodium chloride and yield a sodium compound capable of reacting with a second molecule of benzyl chloride. He concludes that the direct exchange of metal is not possible.[1]

There are, however, other explanations of the above processes not involving addition. The change of O compound to C-compound might occur after substitution under certain conditions, although ethoxycrotonic and ethoxyfumaric ester are comparatively stable

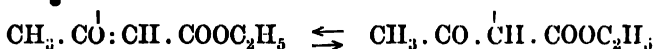


substances, and it is not probable that in these two cases such a shifting of the alkyl group is likely to occur. The acyl derivatives of acetoacetic ester, on the other hand, are known to undergo isomeric change of this character (Part II, p. 363).

Dismissing the theory of isomeric change after replacement as improbable, there is another view which has been advanced by W. Wislicenus.[2] Direct substitution of metal by radical occurs under constraint, and is usually effected by means of an insoluble compound (silver salt) in a non-dissociating medium (ether, benzene, &c.). Replacement by a metal (alkali) in a dissociating solvent and at a higher temperature brings about a 'free reaction', and with it

[1] *Annalen*, 1891, 266, 116.
[2] 'Tautomerie', Ahrens' *Vorträge*, 1898, 2, 249.

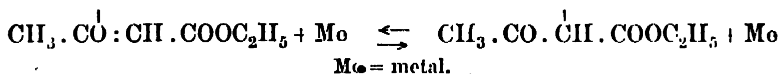
indirect substitution. This latter effect is supposed to depend upon the reversible nature of the free bond of the organic residue on removal of the metal, which may be expressed in the case of acetoacetic ester as follows:



and it will thus enable the C-derivative to be formed. The first, or constrained process, produces an O-derivative; the second, or free reaction, a C-derivative.

But if the formation of an O-derivative in acetoacetic ester depends on a constrained reaction, it is difficult to account for the fact, discovered by Lander,[1] that 90 per cent. of C-ether is formed by the action of ethyl iodide in presence of silver oxide (which gives much the same result as the silver compound).

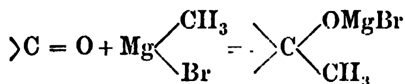
Perhaps the most satisfactory explanation, as suiting the most varied conditions has been supplied by Lapworth (Part II, p. 354), in which there is an equilibrium established between the dissociated ions of the two metallic derivates, or, in other words, an equilibrium mixture of both metallic compounds is present:



Me = metal.

which may shift from one side to the other according to the conditions of the reaction or nature of the reagent or both.

Primarily, no doubt, electrochemical influences prevail, and determine combinations such as occur in the use of zinc alkyls and the Grignard reagents. Michael would probably interpret these reactions by supposing the electropositive metal to link itself to oxygen in a ketone, or to nitrogen in a cyanide, and by neutralising the electronegative effect of oxygen or nitrogen render the adjoining carbon more disposed to polymerise (attach itself to carbon), and thus attract an alkyl group.

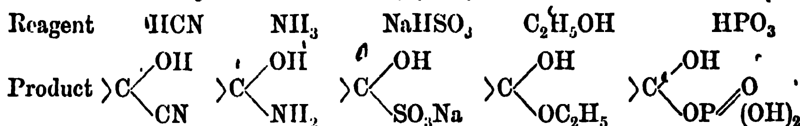


This example introduces a fourth type of addition in which the atoms constituting both unsaturated molecule and molecule of addendum are dissimilar.

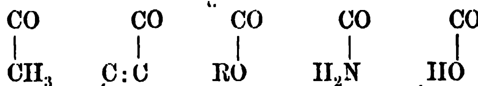
Examples of this type are very common, and may be briefly

[1] *Trans. Chem. Soc.*, 1903, 83, 420.

enumerated. The addition products of *aldehydes and ketones*, C:O, also of *thialdehydes* and *thioketones*, (C:S), are as follows:

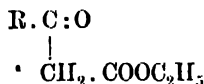


This additive power of the CO group falls away in something like the following order, depending upon the nature of the attached groups:[1]



Similar observations have been made by Goldschmidt[2] on the addition of ammonia to ketonic esters.

In compounds of the general formula,



the stability of the additive product decreases with increasing positivity of R in the following order:



Petrenko-Kritschenko[3] and Stewart[4] have shown that with increasing negativity of the neighbouring groups the reactive power of CO for sodium bisulphite increases; with positive groups it decreases. The following percentages were obtained in thirty minutes with the same strength of solution of sodium bisulphite:[5]

Acetone	47	Pinacoline	5·6
Methyl ethyl ketone	25·1	Acetoacetic ester	56·0
Methyl isopropyl ketone	7·5	Acetone dicarboxylic ester	61·0

Among other unsaturated organic compounds which are capable of forming additive compounds under conditions, which have not been submitted to very careful or systematic examination, are the oximes $\rangle C:NOH$, the methyleneimides $-N:CH_2$, the azoimides

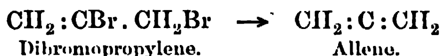


The next class of unsaturated compounds to which attention will be directed is that in which more than one double bond is present. This class may be subdivided into two groups: one in which the unsaturated atoms are similar and adjoin one another,

[1] Vorländer, *Annalen*, 1903, 341, 9.
[2] *Ber.*, 1896, 29, 105.
[3] *Annalen*, 1905, 341, 150.
[4] *Trans. Chem. Soc.*, 1905, 87, 186.
[5] As the numbers refer to the quantity formed in a given time and not to the reaction velocity, they are not strictly comparable.

and have consequently a carbon atom in common, as in allene $CH_2:C:CH_2$, and carbon suboxide $CO:C:CO$, or in which the unsaturated atoms are different, as in ketene and its derivatives, $CH_2:C:O$; and one in which the unsaturated atoms are separated by one or more carbon atoms.

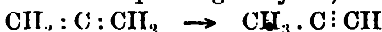
Members of the allene series are very few in number, and have been little studied. They are obtained by the action of metals on the dibromo-olefines and removal of bromine as metallic bromide.



$$CH_2:CBr.CH_2Br \longrightarrow CH_2:C:CH_2$$

Dibromopropylene. Allene.

In presence of sulphuric acid they take up the elements of water and form ketones, and further undergo isomeric change, on heating with sodium, into the corresponding acetylide,



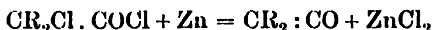
$$CH_2:C:CH_2 \longrightarrow CH_3.C\vdots CH$$

The Ketenes, Carbon Suboxide (C_3O_2). The class of compounds known as ketenes have the general formula $R_2C:CO$. They not only serve to illustrate the various types of reactions characteristic of unsaturated compounds, but afford an insight into the increased reactivity produced by the adjoining double bond on the ketone group. The parent substance, $CH_2:CO$, was obtained by Wilsmore[1] by heating acetic anhydride, acetic ester, or acetone by means of a glowing platinum wire, and by Schmidlin[2] by passing the vapour of acetone through a red-hot tube.



$$CH_3.CO.CH_3 = CH_2:CO + CH_4$$

Staudinger[3] obtained various ketene derivatives, such as methylketene $CH_3.CH:CO$, dimethylketene $(CH_3)_2C:CO$, phenylketene $C_6H_5CH:CO$, and diphenylketene $(C_6H_5)_2C:CO$, by acting upon the halogen acid chloride or bromide with zinc.



$$CR_2Cl.COCl + Zn = CR_2:CO + ZnCl_2$$

Carbon suboxide C_3O_2, which may be included in the same group of unsaturated ketones, was obtained by Diels and Wolf[4] by distilling *in vacuo* a mixture of malonic acid or its ester with phosphorus pentoxide,



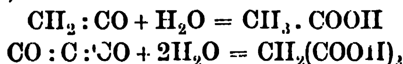
$$CH_2(COOH)_2 = CO:C:CO + 2H_2O$$

or by acting on dibromomalonyl chloride with zinc filings. Both ketene and carbon suboxide are colourless and poisonous gases, with an unpleasant and penetrating smell. Ketene can be liquefied at $-56°$, carbon suboxide at 7°. Staudinger divides the other ketenes into aldoketenes of the formula $RCH:CO$ and ketoketenes $R_2C:CO$.

[1] *Trans. Chem. Soc.*, 1907, **91**, 1938. [2] *Ber.*, 1910, **43**, 2821.
[3] *Die Ketene*, by H. Staudinger. Enke, Stuttgart, 1912.
[4] *Ber.*, 1906, **39**, 689.

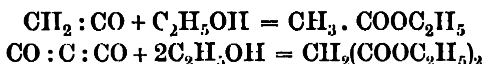
The former are colourless, the latter yellow or orange gases or liquids. They are all extremely reactive, uniting not only with the usual addenda characteristic of ethenoid compounds, such as the halogen acids and halogens, forming acid chlorides and halogen acid chlorides, but also with water, alcohols, mercaptans, primary and secondary amines and acids. In none of these reactions, however, do they resemble true ketones, but rather compounds of the carbimide type CO : NR.

With water, ketene and carbon suboxide form respectively acetic and malonic acid,



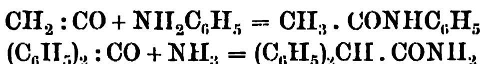
$$CH_2 : CO + H_2O = CH_3 . COOH$$
$$CO : C : CO + 2H_2O = CH_2(COOH)_2$$

With alcohol, they yield acetic and malonic ester,



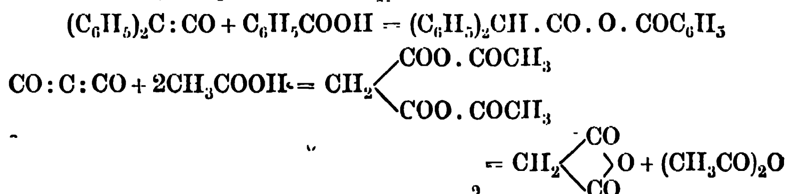
$$CH_2 : CO + C_2H_5OH = CH_3 . COOC_2H_5$$
$$CO : C : CO + 2C_2H_5OH = CH_2(COOC_2H_5)_2$$

With aniline or ammonia, the ketenes yield anilides or amides,



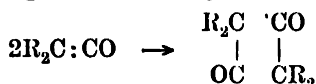
$$CH_2 : CO + NH_2C_6H_5 = CH_3 . CONHC_6H_5$$
$$(C_6H_5)_2 : CO + NH_3 = (C_6H_5)_2CH . CONH_2$$

With acids, anhydrides are formed,



$$(C_6H_5)_2C : CO + C_6H_5COOH = (C_6H_5)_2CH . CO . O . COC_6H_5$$
$$CO : C : CO + 2CH_3COOH = CH_2\left\langle\begin{matrix} COO . COCH_3 \\ COO . COCH_3 \end{matrix}\right.$$
$$= CH_2\left\langle\begin{matrix} CO \\ CO \end{matrix}\right\rangle O + (CH_3CO)_2O$$

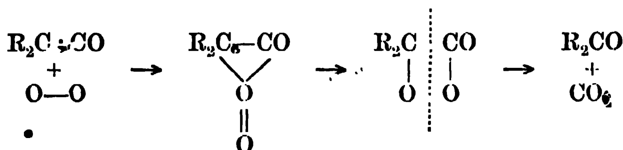
A second type of reaction is presented by the union of two or more molecules of ketene; in other words, by polymerisation. Whilst the ketoketenes are more disposed to form additive compounds, the aldoketenes are characterised by their remarkable tendency to polymerise. In the latter case polymerisation takes place so rapidly, even in dilute solutions, that the aldoketenes cannot be prepared in a pure state. The ketoketenes polymerise more slowly, dimethylketene requiring from one to two hours at the ordinary temperature, whilst diphenylketene will remain unchanged for months. Spontaneous polymerisation, that is, at the ordinary temperature and without the use of reagents, leads to cyclobutane derivatives:



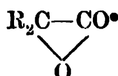
$$2R_2C : CO \longrightarrow \begin{matrix} R_2C & CO \\ | & | \\ OC & CR_2 \end{matrix}$$

A third type of reaction is illustrated by the formation of an additive compound followed by cleavage into two new molecules.

This is best shown by the behaviour of oxygen, with which more especially the ketoketenes unite. By passing oxygen into dimethyl- or diethyl-ketene at $-20°$, white amorphous compounds separate which in the dry state explode violently; but suspended in ether they break up into carbon dioxide and the ketone

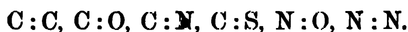


The reason for introducing a second intermediate dioxide stage between ketene and ketone is the existence of ketene oxides of the formula,



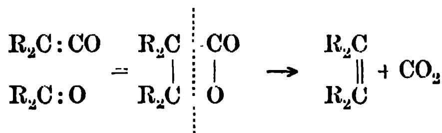
which in the case of phenylmethylketene and diphenylketene appear in considerable quantity along with the dioxide.

Finally, there is a fourth type of reaction illustrated by the union of the ketene with a second unsaturated molecule, containing one of the following groups:

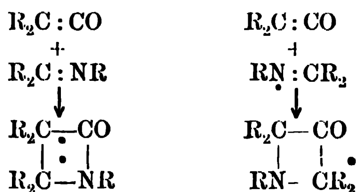


A four-atom ring is first produced, which more or less easily breaks down into two new molecules.

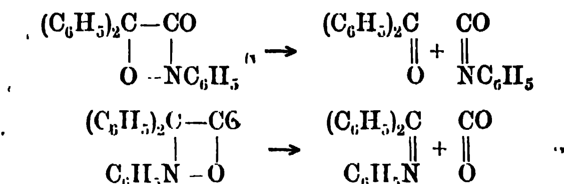
With ketones, for example, the following reaction takes place:



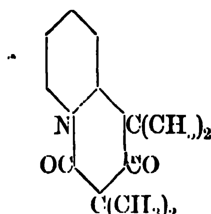
The addition may occur in two ways, and it has actually been observed in the case of the compounds with the carbimides thus:



Where union with nitroso compounds occurs, such as diphenylketene with nitrosobenzene, combination and cleavage follow two directions:

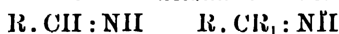


Thus every type of reaction is represented, and it should be observed that in addition to the foregoing, additive compounds are formed with pyridine and quinoline, acid chlorides, hydrogen cyanide, and the Grignard reagent, yet in no case is the behaviour that of a true ketone. This difference in character may be ascribed to the presence of two adjoining double bonds, which not only enhance the reactivity of the molecule, but fundamentally alter the ketonic character of the substance.



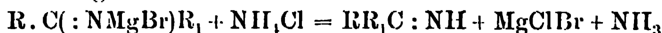
Dimethylketene-pyridine.

A group of compounds termed *ketimines* of the general formulae



$$R.CH:NH \qquad R.CR_1:NH$$

have more recently been obtained by Moureu and Mignonac[1] by the action of ammonium chloride on the product of the action of the Grignard reagent on the nitriles



$$R.C(:NMgBr)R_1 + NH_4Cl = RR_1C:NH + MgClBr + NH_3$$

They are low-boiling basic substances which combine with acids forming crystalline salts, readily decomposed by water into the ketone and ammonium chloride



$$RR_1C:NH_2Cl + H_2O = RR_1CO + NH_4Cl$$

Conjugated Double Bonds. This term has been applied to those unsaturated compounds in which the unsaturated groups have no single carbon atom in common, but the pairs of double bonds are separated as in isoprene or butadiene, acrolein or glyoxal.



$CH_2:C(CH_3).CH:CH_2$ Isoprene. $CH_2:CH.CH:CH_2$ Butadiene. $CH_2:CH.CH:O$ Acrolein.



$O:CH.CH:O$ Glyoxal.

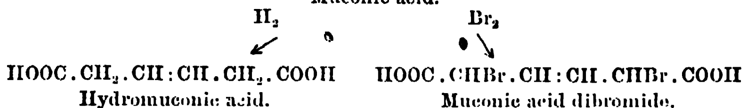
[1] *Comp. rend.*, 1913, 156, 1801.

Under certain conditions of atomic environment such a grouping of double bonds exhibits abnormal chemical behaviour and abnormal physical properties. For example, muconic acid on reduction or bromination does not unite with four atoms of each element, as the existence of two pairs of double bonds might lead one to expect, but only two atoms are absorbed, and attach themselves to the α carbon atoms at either end of the chain, a process which is accompanied by a shifting of the double bond to the middle position.[1]



$$HOOC.CH:CH.CH:CH.COOH$$

Muconic acid.

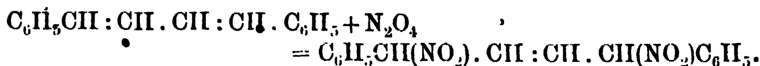


H_2 ↙ ↘ Br_2

$$HOOC.CH_2.CH:CH.CH_2.COOH \qquad HOOC.CHBr.CH:CH.CHBr.COOH$$

Hydromuconic acid. Muconic acid dibromide.

Similarly, diphenylbutadiene unites with nitrogen tetroxide to form a 1.4 dinitro compound.[2]



$$C_6H_5CH:CH.CH:CH.C_6H_5 + N_2O_4 = C_6H_5CH(NO_2).CH:CH.CH(NO_2)C_6H_5.$$

That the positive hydrogen atoms should seek the most negative carbon atoms is not surprising, and these are situated at the end of the chain; but that the negative bromine atoms and nitro groups should act similarly introduces a difficulty for which an electrochemical explanation seems insufficient. Moreover, there is no apparent reason why, supposing the first two atoms to enter the end positions in the chain, reduction or bromination should stop, as it does.

Thiele's Theory. To account for this and similar phenomena J. Thiele[3] has introduced his theory of *partial valencies*.

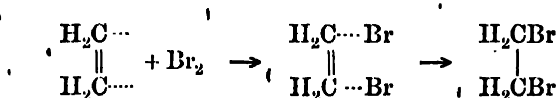
According to Thiele the valency of unsaturated atoms, which are usually denoted by double or treble linkages, is not wholly utilized, but some force of affinity remains as a residual or partial valency, by virtue of which the process of addition is initiated. These partial valencies are indicated by dotted lines.



$$C=C \qquad C=O \qquad C=N \qquad N=N$$

Ethylene, for example, attaches bromine in the first instance by its partial valencies, which change to a full valency simultaneously with the appearance of a single linkage in place of the double bond.

[1] *Annalen*, 1883, 216, 171; 1885, 227, 46; 1889, 251, 257; 1890, 256, 1.
[2] Straus, *Ber.*, 1909, 42, 2866.
[3] *Annalen*, 1899, 306, 87.



The electrochemical nature of the elements determines the process of addition; for example, N=N has no affinity for chlorine and no addition of this element occurs; hydrogen unites with oxygen rather than with carbon, the acid radical with carbon rather than with hydrogen, and so forth.

The existence of residual affinity in unsaturated atoms agrees with Thomsen's[1] calculation of the thermal value of an ethylene bond, which he finds less than that of two single linkages.

Passing to the case of two adjoining pairs of double linkages referred to at the beginning of this section, Thiele supposes the central pair of partial valencies to neutralize one another and lose their activity like the opposite poles of two magnets when made to touch. The union is indicated by a curved line and is termed *conjugated*, and the whole arrangement a *conjugated double bond*. In this way the partial valencies of only the end atoms remain active and capable of attaching new atoms, whilst the conjugated atoms are inactive.

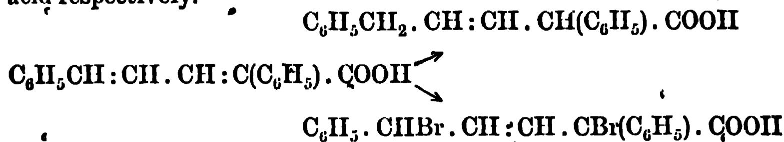


Compounds with conjugated double bonds are therefore more saturated and, as we shall see later (Part II, p. 67), have a smaller heat of combustion. The same thing is supposed to occur in unsaturated ketones and in diketones and acids.



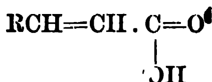
As soon as addition has taken place the conjugated bond changes into a normal double bond, and in this way reduction or bromination of the end carbon atoms is effected.

The following are a few examples. Phenylcinnamylacrylic acid gives on reduction and bromination the 1.4 dihydro and dibromo acid respectively.[2]



The $\alpha\beta$ unsaturated acids with the conjugated grouping

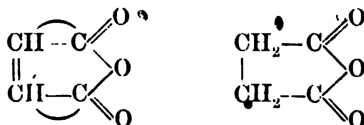
[1] *Zeit. physik. Chem.*, 1887, 1, 369. [2] *Annalen*, 1899, 306, 201.



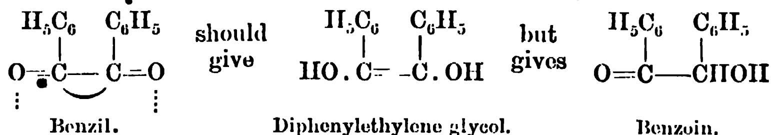
do not unite with bromine as readily or as rapidly as the $\beta\gamma$ acids

$$RCH{=}CH.CH_2.C{=}O \atop {\quad\quad\quad\quad\quad\quad | \atop \quad\quad\quad\quad\quad\quad OH}$$

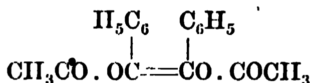
, which are unconjugated and therefore less saturated. The rate of hydration of saturated and unsaturated anhydrides shows great differences, which are ascribed to conjugation. Maleic acid, which contains conjugated double bonds, undergoes hydration ten times as quickly as succinic anhydride.[1]



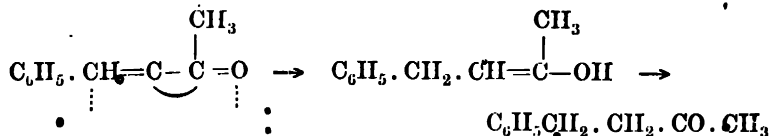
According to Thiele's theory benzil should give on reduction diphenylethylene glycol, whereas benzoin is actually formed.



How is this to be explained? Thiele attributes the final stage to isomeric change of the very labile intermediate product. Supposing, however, reduction to be effected in presence of acetic anhydride and sulphuric acid, the acetyl derivative of the intermediate glycol should be formed and isomeric change arrested. This is precisely what happens. Two stereoisomeric diacetates of diphenylethylene glycol are formed.



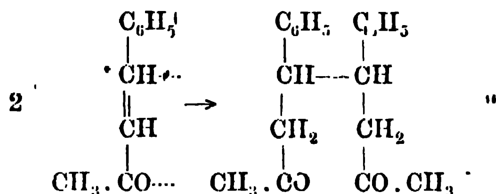
Similarly, benzylidene acetone should give hydrocinnamyl methyl ketone in place of the unstable alcohol.



But Harries finds that the reaction proceeds otherwise, and that

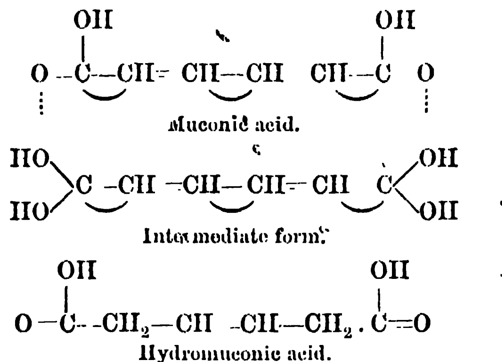
[1] Rivett and Sidgwick, *Trans.*, 1910, 97, 1677.

two molecules of benzylidene acetone join up to form a saturated double ketone.

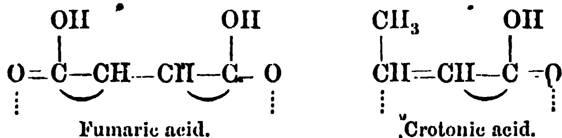


The reaction is explained by supposing that the electronegative oxygen first unites with hydrogen, and the alcohol thus formed isomerises to the ketone form. This leaves the partial valencies of the carbon free to unite with hydrogen or with a second molecule, and it is the latter process which occurs.

The reduction of muconic acid is also readily explained. As it contains three conjugated linkages only the end oxygen atoms possess partial valencies and the end groups $C\langle^{OH}_{OH}$ isomerise to carboxyl by passing on an atom of hydrogen to the α carbon.



The theory explains, moreover, in a simple fashion why fumaric acid is more easily reduced than crotonic acid, since electropositive oxygen attaches hydrogen more readily than carbon.



This may also explain why the halogen enters the β position, where halogen acid combines with an unsaturated acid. In acrylic acid,

for example, the hydrogen attaches itself to oxygen and the bromine to carbon.

$$\underset{\text{Acrylic acid.}}{CH_2{=}CH{-}\overset{\displaystyle OH}{\overset{|}{C}}{=}O} \rightarrow \underset{\displaystyle Br}{\overset{}{\underset{|}{CH_2}}}{-}CH{=}C\begin{smallmatrix}OH\\OH\end{smallmatrix} \rightarrow \underset{\beta\text{-Bromopropionic acid.}}{CH_2Br.CH_2.CO.OH}$$

In the same way, when addition of water or ammonia takes place, OH and NH_2 unite with the β carbon and hydrogen to the α carbon. It is not therefore due to the negative addendum being repelled by the negative carboxyl group, as frequently assumed. Ammonia combines with phorone thus:

$$\underset{\text{Phorone.}}{\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}{>}C{:}CH{-}CO.CH{:}C{<}\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}} \rightarrow \begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}{>}\underset{\displaystyle NH_2}{\underset{|}{C}}{-}CH_2{-}CO.CH{:}C{<}\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}$$

Thiele's theory also explains the addition of magnesium acyl or alkyl bromide to unsaturated ketones and esters; but the position taken by the radical is here found to depend on the nature of the radical already associated with the ketone or ester group. In the case of cinnamic ester, a phenyl or cyanogen group attached to the α carbon will cause the acyl group to attach itself to the β carbon, in the case of a methyl group to the α carbon.[1]

Crossed Double Bonds. An example of what are termed crossed double bonds occurs in dibenzalpropionic acid.

$$\overset{1}{C_6H_5CH}{=}\overset{2}{C}{-}\overset{3}{CH}{=}\overset{4}{CH}.C_6H_5 \\ \qquad | \\ \qquad C{=}O \\ \qquad | \\ \qquad OH$$

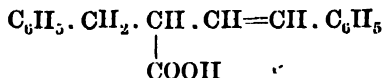
Here it will be observed that a conjugated system may be formed between the different pairs of carbon atoms.

$$C_6H_5CH{=}C{-}CH{=}CH.C_6H_5 \\ \qquad | \\ \qquad C{=}O \\ \qquad | \\ \qquad OH$$

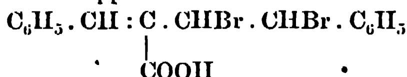
Such an arrangement presents two alternative ways in which addition may occur, the nature of the product depending on that of the

[1] Kohler, *Amer. Chem. Journ.*, 1905, 36, 529; 1906, 37, 369; 1907, 38, 511.

addendum. In the case of bromine it is scarcely surprising to find that it attaches itself to carbon atoms 1, 4. Hydrogen and halogen acid, on the other hand, distribute themselves between oxygen and the nearest carbon atom. With hydrogen the following compound is formed:



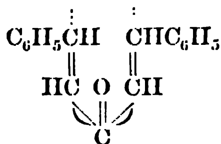
It should, however, be pointed out that in addition to the 1.4 dibromo-additive compound, a second, 3.4, compound is also produced. How is the latter accounted for? Thiele lays emphasis on the fact that the partial valency of the central carbon, 2, by being distributed between its two neighbours, does not neutralise their activity, and some is available for additive purposes. Hence the dibromo derivative appears:

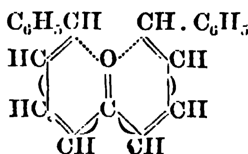


Borsche[1] has recently shown that the union of ethyl acetoacetate with certain ketones containing a system of crossed double linkages

O
||
C:C.C.C

depends on the length of the chain. If the chain is sufficiently long the ends may approach one another so closely that a part of the residual affinity is saturated, and will not unite with the ester. This is the case with dicinnamylidene acetone, but not with distyryl ketone.

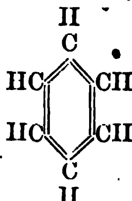




Sufficient has been said to indicate the general nature of the theory, and the resources available for meeting apparent anomalies. Before discussing the exceptions to the theory, it may be well to consider its application to the aromatic series of compounds. Its application to the benzene formula is fully discussed (Part II, chap. vii), and little more need be said on the subject. In reference to it Thiele says: 'as by the neutralisation of the partial valencies the original three double bonds vanish, no distinction can be drawn between them and the secondary (conjugated) double bonds. Benzene contains six inactive double bonds. Thus, the difficulty presented by the two ortho positions, 1.2 and 1.6, which

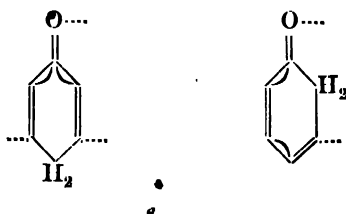
[1] *Annalen*, 1910, 375, 145.

Kekulé attempted to meet by the aid of his dynamic hypothesis, disappears. Benzene may be, therefore, represented by the formula,

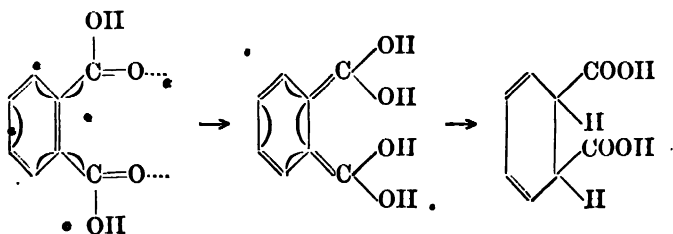


if it is desired to attach weight to its saturated character and to the equality of the ortho positions.'

Thiele has applied the theory in a variety of ways to explain certain characteristics of benzene derivatives. Phenol, for example, is distinguished by its high reactivity, which it loses to some extent in its ethers and esters.[1] Assuming that it may react in its isomeric form of ketone, the partial valencies will at once come into play.

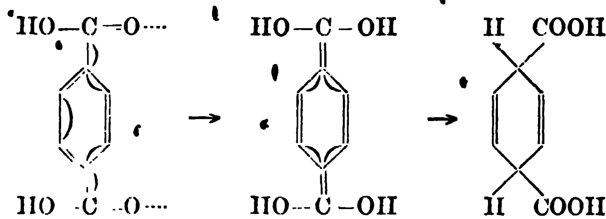


The reduction of the aromatic acids (see Part II, p. 397) may be considered from the same point of view as that of muconic acid (p. 133). On the reduction of terephthalic and phthalic acids, the hydrogen attaches itself to the α carbon atoms.



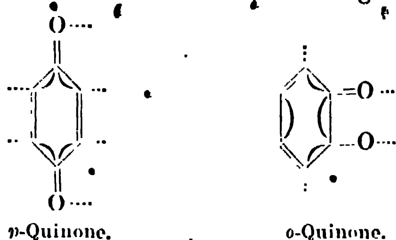
Reduction of Phthalic acid.

[1] That the phenols show greater reactivity than their ethers, and that they react in the ketone rather than in the enol form, has been questioned. K. H. Meyer and Lenhardt, *Annalen*, 1913, 398, 66.



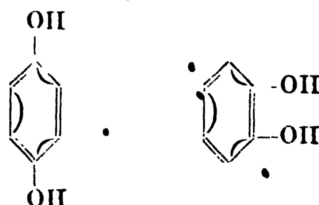
Reduction of Terephthalic acid.

The quinones furnish an interesting case, because addition may occur in different positions, and the differences observed may be ascribed to the nature of the entrant atoms and groups.

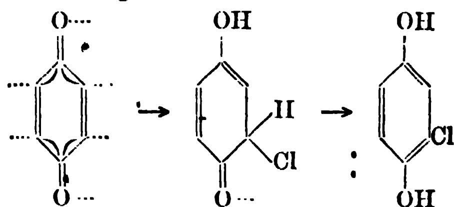


p-Quinone. o-Quinone.

Hydrogen attaches itself to oxygen, and quinol and catechol result.

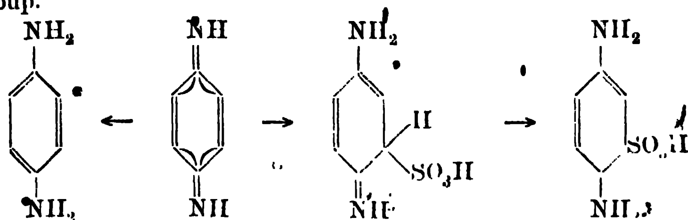


That reduction is arrested at this stage naturally follows. Halogens, on the other hand, will seek the carbon atoms and di- and tetrachloroquinones will be formed. Halogen acid will distribute itself between the oxygen and the nuclear carbon, and, according to Thiele, will pursue the following course :

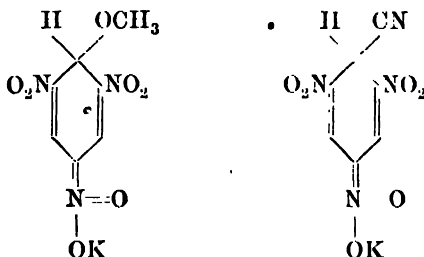


The quinonimines will act in a similar fashion. Quinonediimine on reduction should produce p-phenylenediamine, whilst sulphurous acid should react like hydrogen chloride, the acid group remaining

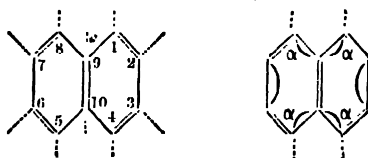
attached to the nucleus, and the hydrogen passing to the imino group.



Meisenheimer[1] has utilized the idea of partial valencies in order to explain certain reactions of nitro compounds, such, for example, as the formation of alkali salts of trinitrobenzene and trinitrotoluene in alcoholic solution, and their combinations with potassium cyanide.

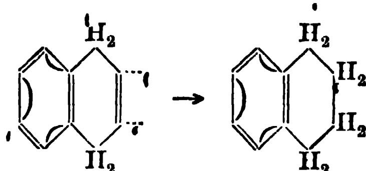


In naphthalene the distribution of partial valencies and their conjugation will appear as follows :

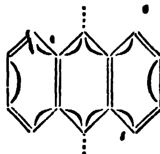


The partial valencies of the two central carbon atoms will not suffice to neutralise those in the α positions, and consequently they are the most easily attacked ; for it is well known that substitution takes place in these positions. Supposing that on reduction hydrogen enters positions 1.4, what will be the effect? The *half* partial valencies of the two central carbon atoms will be withdrawn from this pair, and consequently those directed towards 5.8 will be *full* partial valencies, or, in other words, the unreduced ring will be transformed into a true benzene ring, whilst the other ring can take up two further hydrogen atoms, as Bamberger has found (Part III, p. 283).

[1] *Annalen*, 1902, **323**, 219, 241.



Anthracene in the same way may be represented by the formula:



Thiele claims for this formula the advantage that it explains the well-known reactivity of the para-carbon atoms of the central nucleus, a view which has been developed by Meisenheimer[1] in relation to the nitro-derivatives.[2]

Phenanthrene has the formula,



which explains the peculiar reactivity of the HC=CH group.

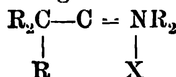
The effect of conjugation is not manifested only by chemical behaviour, but is seen in the enhanced optical activity, magnetic rotation, and refractivity described in Part II, pp. 28, 53, and 223.

An interesting extension of Thiele's theory has been brought forward by Robinson and Hamilton.[3] From their own and Decker's observations[4] they conclude that tervalent nitrogen may act as a member of a conjugated system. They have been able to show that where the group



$$R_2C = C{-}NR_2 \qquad (R_2 = \text{alkyl or H})$$

occurs, whether the nitrogen forms part of a chain or ring, both alkyl salts (alkyl acid sulphates and alkyl iodides) attach themselves to the end atoms, the alkyl group (R) joining the carbon atom and the negative group (X) the nitrogen with the usual change of linkage



This may take the form of direct addition or lead to a secondary process of hydrolysis, as illustrated by the behaviour of β-diethyl-

[1] *Annalen*, 1902, **323**, 204.

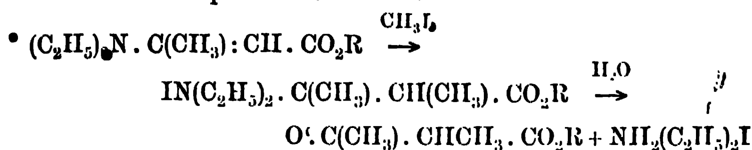
[2] It should be pointed out that, though there may be more free valency at the disposal of the two central carbon atoms, the para-carbon atoms in the two side rings are in a condition precisely similar to those in the α positions in naphthalene.

[3] *Trans. Chem. Soc.*, 1916, **109**, 1029, 1038; 1917, **111**, 958.

[4] *Ber.*, 1904, **37**, 523; 1905, **38**, 2893.

aminocrotonic ester with alkyl iodides giving, by hydrolysis with water, methylacetoacetic ester.

The action is explained as follows:



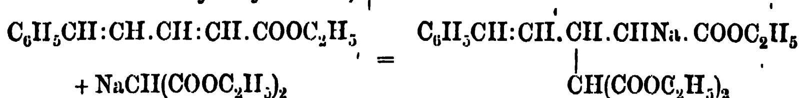
$$(C_2H_5)_2N . C(CH_3) : CH . CO_2R \xrightarrow{CH_3I} IN(C_2H_5)_2 . C(CH_3) . CH(CH_3) . CO_2R \xrightarrow{H_2O} O : C(CH_3) . CHCH_3 . CO_2R + NH_2(C_2H_5)_2I$$

To explain the behaviour of nitrogen in this addition process, the authors consider that it possesses (in addition to two latent valencies) two partial valencies, and that the normal valency of every atom may be accompanied by a partial valency. They deduce a number of interesting results from this theory, and suggest that oxygen possesses partial valencies, thus explaining the formation of alkyl derivatives of acetoacetic ester by the attachment of iodine of the alkyl iodide to oxygen and the methyl group to carbon of the sodium compound.

Like most chemical theories, that of Thiele has become an attractive target for the shafts of criticism. It has been attacked by Michael, Hinrichsen, Erlenmeyer, and others on the ground that it is not only unnecessary, but that the numerous exceptions which have been observed render it untenable. Michael[1] accuses its author of adopting or discarding, as may suit his purpose, the positive-negative rule (see p. 113). He points out that Thiele assumes that in certain cases the atoms or groups of the addendum distribute themselves according to their electrochemical character, but that the addition of halogen acids and ammonia to unsaturated acids is based on an entirely different conception. Again, in dibenzalpropionic acid (p. 137), the two carbon atoms with the strongest partial valencies are 1.4, and consequently the 1.4 dibromo acid should of the two be formed in larger quantity, whereas the 3.4 dibromo compound predominates. These and other additive processes find, according to Michael, a readier explanation by the aid of the positive-negative rule. Hinrichsen,[2] like Michael, assails the theory on the ground that it attaches too little weight to the electrochemical nature of the additive process; 'the constitution of a substance produced by the addition of atoms and radicals to unsaturated compounds is determined in the first place by the qualitative relationship existing between the addendum on the one hand and the atoms or atomic groups present in the unsaturated molecule on the other.' Among the many exceptions to Thiele's theory the following may be cited:

[1] *J. Prakt. Chem.*, 1899, 60, 467.
[2] *Annalen*, 1904, 336, 171.

Michael's reaction (p. 202) and the addition of sodium malonic ester to cinnamylacrylic ester,[1]



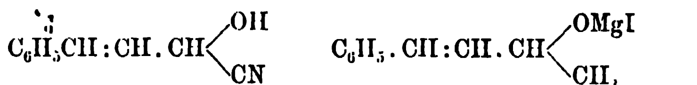
$$C_6H_5CH:CH.CH:CH.COOC_2H_5 + NaCH(COOC_2H_5)_2 = C_6H_5CH:CH.CH.CHNa.COOC_2H_5 \; (CH(COOC_2H_5)_2)$$

the addition of bromine to cinnamic acid, which follows the normal course, the reduction of cinnamylformic acid to phenyl-α-hydroxy-isocrotonic acid,[2]



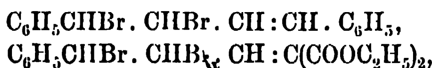
$$C_6H_5CH:CH.CO.COOH \rightarrow C_6H_5CH:CH.CH(OH).COOH,$$

the addition of hydrogen cyanide and magnesium methyl iodide to the CO group of cinnamic aldehyde,[3]



$$C_6H_5CH:CH.CH\langle^{OH}_{CN} \qquad C_6H_5.CH:CH.CH\langle^{OMgI}_{CH_3}$$

the addition of bromine to diphenylbutadiene[4] and to cinnamylidene-malonic ester, both of which yield 1.2 dibromides,



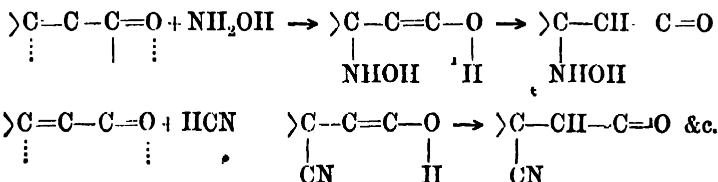
$$C_6H_5CHBr.CHBr.CH:CH.C_6H_5,$$
$$C_6H_5CHBr.CHBr.CH:C(COOC_2H_5)_2,$$

and the reduction of dibenzalpropionic acid, which also gives a 1.2 dihydro derivative,



$$C_6H_5CH:CH.CH(CO_2H).CH_2.C_6H_5.$$

Apparent exceptions in the case of 1.2 additive compounds of unsaturated ketones and esters with ammonia,[5] hydroxylamine,[6] hydrogen cyanide,[7] and sulphurous acid[8] may be explained on Thiele's theory by including the CO of the carboxyl group in the conjugated series, and assuming isomeric changes to follow thus:

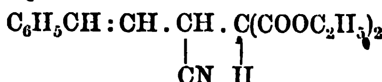


$$>C-C-C=O + NH_2OH \rightarrow >C-C=C-O \rightarrow >C-CH-C=O$$
(with NHOH and H added: NHOH, H, NHOH)

$$>C=C-C=O + HCN \quad >C-C=C-O \rightarrow >C-CH-C=O \;\&c.$$
(with CN, H, CN)

[1] Vorländer, *Ber.*, 1903, 36, 2339.
[2] Erlenmeyer, jun., *Ber.*, 1903, 36, 2529; 1904, 37, 1318.
[3] Kohler, *Am. Chem. J.*, 1904, 31, 642; 1905, 33, 153, 333; 1907, 36, 529.
[4] Straus, *Ber.*, 1909, 42, 2866; Riiber, *Ber.*, 1911, 44, 2974.
[5] Kœhl and Dinter, *Ber.*, 1903, 36, 172.
[6] Harries, *Ber.*, 1897, 30, 230; 1904, 37, 252. Posner, *Ber.*, 1903, 36, 4305; 1907, 40, 218, 227; 1909, 42, 2785. Riedel and Schulz, *Annalen*, 1909, 367, 14.
[7] Lapworth, *Trans. Chem. Soc.*, 1903, 83, 995; 1904, 85, 1214. Knoevenagel, *Ber.*, 1904, 37, 4065.
[8] Tiemann, *Ber.*, 1898, 31, 3297; Knoevenagel, *Ber.*, 1904, 37, 4038.

Thiele and Meisenheimer,[1] who obtained the hydrogen cyanide compound of cinnamylidene malonic ester,

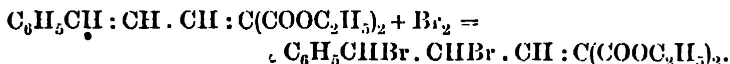


$$C_6H_5CH:CH.CH.C(COOC_2H_5)_2 \quad (CN, H)$$

admitted that it constituted an exception to the theory, and, if this is so, others may be included in the same category.

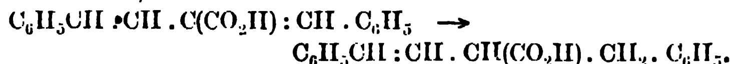
Hinrichsen[2] has formulated the additive process on the basis of Michael's positive-negative rule in the following series of simple propositions:

Addition is determined by the electrochemical nature of the unsaturated groups as well as by that of the constituents of the addendum. If the latter are of opposite polar character, as $H.Br$, $H.CN$, $K.HSO_3$, $H.NH_2$, $Na.HC(COOC_2H_5)_2$, $Na.OC_2H_5$, $C_6H_5CH_2S.H$, $H.NHOH$, the mutual attraction of the constituent atoms or groups will direct them to adjoining atoms, i.e. to the 1.2 position. If, on the other hand, the constituents of the addendum are the same, H_2, Br_2, N_2O_4, two conditions may obtain; either mutual repulsion may drive them apart into positions 1.4, or the opposite polar character of the unsaturated groups may counteract the mutual repulsion of the constituents of the addendum, and cause the latter to enter positions 1.2, as in cinnamylidene malonic ester,



$$C_6H_5CH:CH.CH:C(COOC_2H_5)_2 + Br_2 = C_6H_5CHBr.CHBr.CH:C(COOC_2H_5)_2.$$

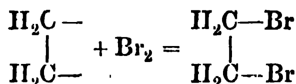
If, finally, each unsaturated group in position 1.2 is oppositely polar to each constituent of the addendum, the mutual attraction may cause the latter to enter positions 1.2 instead of driving them apart. Thus, on reducing dibenzalpropionic acid, the two positive hydrogen atoms are attracted to the two negative groups in positions 1.2,



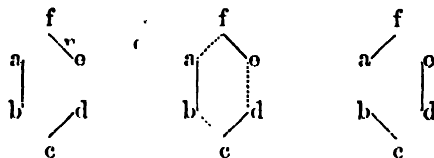
$$C_6H_5CH:CH.C(CO_2H):CH.C_6H_5 \longrightarrow C_6H_5CH:CH.CH(CO_2H).CH_2.C_6H_5.$$

The addition in positions 1.4 generally occurs under special conditions. Erlenmeyer, jun.,[3] like Hinrichsen, considers that the principle of free valencies in the case of unsaturated compounds serves the purpose better than that of Thiele's partial valencies, and that the union of ethylene and bromine may be expressed thus:

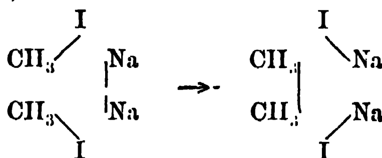
[1] *Annalen*, 1899, **306**, 247. [2] *Chem. Ztg.*, 1909, **33**, 1097.
[3] *Annalen*, 1901, **316**, 43; see also Robinson, *Trans. Chem. Soc.*, 1917, **111**, 958.



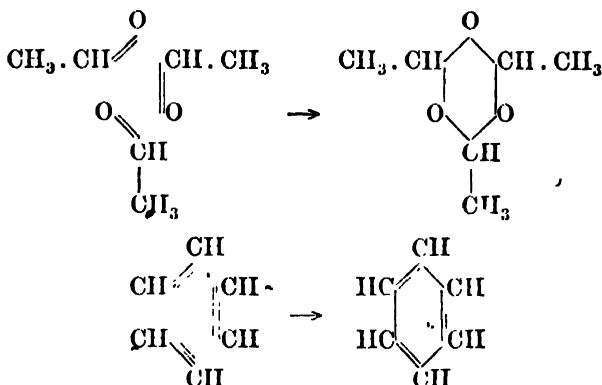
He adopts Kekulé's view (p. 110) that addition must be assumed to precede substitution in saturated compounds, and therefore the theory of partial valencies must logically be extended to them also. Thiele's theory must consequently either be discarded or expanded. Kekulé's scheme does not, however, include all reactions, and to extend its scope Erlenmeyer has added the following:



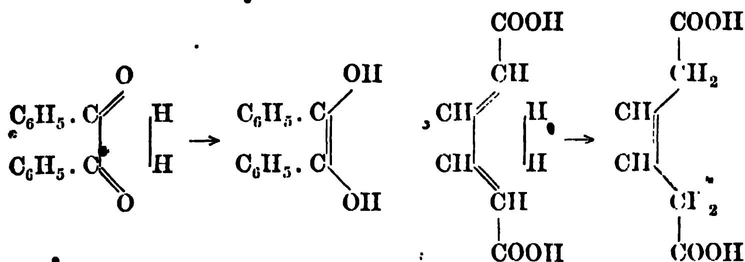
which is intended to convey the notion of the mechanism of the interaction of three reacting groups before, during, and after a reaction, as, for example, the formation of ethane from methyl iodide and sodium,



or the polymerisation of acetaldehyde and acetylene,

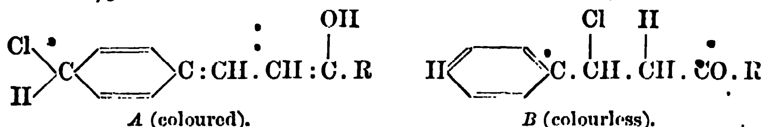


The idea may be applied to the reduction of benzil and muconic acid, when Thiele's theory becomes unnecessary.



According to Erlenmoyer this view of the process has the advantage over Thiele's, inasmuch as it is of general application, and presents a variety of reactions from a common standpoint, without recourse to hypothetical partial valencies. His further attempts, like those of Knoevenagel,[1] to represent the various kinds of chemical combination by phases in the oscillation of carbon tetrahedra, or spheres cannot be regarded as very convincing, and must be left to the reader for reference.

An interesting view of the nature of the addition process, as it occurs in unsaturated ketones, has been described by Vorländer and his collaborators[2] from results of observations by themselves and others on the action of acids (hydrochloric, hydrobromic, sulphuric, phosphoric, and picric acids) and a few halide salts ($HgCl_2$, $FeCl_3$) on certain aromatic $\alpha\beta$ unsaturated ketones containing the group C:C.C:O. They find, for example, that substances such as dibenzalacetone, $C_6H_5CH:CH.CO.CH:CH.C_6H_5$ the corresponding dianisalacetone, &c., form additive compounds with one or two molecules of hydrogen chloride or bromide, or one molecule of sulphuric acid; that benzalacetone, $C_6H_5CH:CH.CO.CH_3$, unites with one molecule of hydrogen chloride, and so forth. This reaction appears to take place in two well-marked phases. In the first phase, an unstable and brightly coloured yellow, orange, or red compound called *A* is formed, which, on the addition of water, easily loses acid and gives the original compound; in the second phase the colour vanishes more or less quickly with the production of a stable, colourless compound, *B*. The authors then discuss the nature of the change. They discard in turn the theory of Kehrmann and Wentzel, who ascribe to *A* and *B* a different structure,



A (coloured). *B* (colourless).

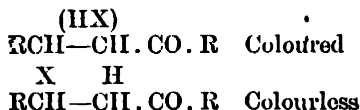
[1] *Annalen*, 1900, 311, 203.

[2] *Ber.*, 1903, 36, 1470, 3528; 1904, 37, 1644; *Annalen*, 1903, 341, 1; 1906, 345, 155.

because, as Baeyer and Villiger[1] have pointed out in the case of dianisalacetone, the methoxyl group in the para position in *A* would be eliminated with the chlorine and yield a quinone, a reaction which does not take place. They also reject the theory of Baeyer and Villiger that the colour is due to the union of the acid with the ketone oxygen, because it has been found in compounds of this class that the CO group is less reactive than the neighbouring C=C group, and such a union would not explain the addition of two molecules of halogen acid to dibenzalacetone, &c. Moreover, an unsaturated compound containing no CO group, such as anethole, isosafrole, &c., forms yellow and red additive compounds with hydrogen bromide and picric acid, and the same occurs with anthracene and phenanthrene. For this and other reasons Vorländer also rejects Thiele's rule of the existence of a 1.4 and 1.2 additive compound. Nor is the colour necessarily due to the formation of a coloured ion, for then trimethylammoniumazobenzene chloride, $C_6H_5N : N . C_6H_4 . N(CH_3)_3Cl$, should be violet, like aminoazobenzene hydrochloride, $C_6H_5N : N . C_6H_4NH_3Cl$, whereas it is orange, like aminoazobenzene. The colour must therefore be due to a change in the saturation capacity of one or more elements.

Vorländer considers the interaction of two substances to depend upon a difference of potential, which falls slightly in the formation of the *A* coloured compounds, but much more in that of the *B* colourless compounds. The first stage in the process of combination corresponding to the *A* compound is compared to two oppositely charged conductors separated by a dielectric, in which the charges are concentrated at opposite points of the conductor; the second, corresponding to the *B* compound, to their discharge on coming into contact. A strain is first set up, followed by a fall of energy in the system. The two phases, *A* and *B*, are termed 'addition isomerism'.

They are represented in the following way: in the first or colour-forming phase there is no separation of the constituents of HX, but the attachment is that of a molecular compound; in the second, dissociation of HX occurs and the two constituents combine additively, with loss of energy, forming the stable and colourless compound.



[1] *Ber.*, 1902, 35, 1191.

If the assumption of the existence of molecular ions is correct, the first reaction will be influenced by the nature of the solvent as well as by temperature, pressure, and the action of light, whereas in the second, the solvent will have little effect.

THE AROMATIC HYDROCARBONS

The aromatic hydrocarbons, standing as it were midway between saturated and unsaturated compounds, may be briefly considered here.

Substitution in the Aromatic Series. It is well known that substitution in the nucleus of a monosubstituted benzene derivative gives rise to one or more isomers. It is rare to find all three present in the product; but usually the new substituent enters either the ortho or para position, or both ortho and para positions, or on the other hand only the meta position. The group already present appears to possess a directing influence, which has been embodied in certain rules of substitution. Hübner[1] expresses it as follows: 'In the replacement of hydrogen in the benzene nucleus the entrant negative (acid) substituent enters the para position and at the same time the ortho position to the least negative or acid substituent already present. It follows from this that if an acid (negative) substituent is already present and a second acid substituent enters, the latter will avoid the ortho and para positions as far as possible and enter mainly the meta position.'

Noelting[2] has expressed the same thing more definitely: 'If a neutral, basic, or weakly acid group, such as CH_3, Cl, Br, I, NH_2, OH, occupies position 1, by the action of Cl, Br, I, HNO_3, and H_2SO_4 the main product will be a para compound together with varying but always smaller quantities of ortho derivatives. But if the position 1 is occupied by an acid group, NO_2, CO_2H, SO_3H, the action of the above reagents produces mainly a meta compound together with small quantities of the ortho and para series.' Crum-Brown and Gibson[3] have presented the rule in a rather different form. Supposing the radical already present forms a compound with hydrogen, which can be converted by direct oxidation into the corresponding hydroxyl compound, the new substituent will enter the meta position, otherwise it will occupy the ortho-para position. Thus HCl cannot be oxidised directly to HClO, but acetaldehyde CH_3CHO gives CH_3COOH. The directing influence of chlorine in

[1] *Ber.*, 1875, 8, 873. [2] *Ber.*, 1876, 9, 1797.
[3] *Trans. Chem. Soc.*, 1892, 61, 367.

the first case is therefore to the ortho-para, that of acetyl to the meta position. The results are given in the form of a table:

C_6H_5Cl	Cl	HCl	HOCl	*o-p*
C_6H_5Br	Br	HBr	HOBr	*o-p*
$C_6H_5CH_3$	CH_3	HCH_3	$HOCH_3$	*o-p*
$C_6H_5NH_2$	NH_2	HNH_2	$HONH_2$	*o-p*
C_6H_5OH	OH	HOH	HOOH	*o-p*
$C_6H_5NO_2$	NO_2	HNO_2	$HONO_2$	*m*
$C_6H_5CCl_3$	CCl_3	$HCCl_3$	$HOCCl_3$	*o-p*
C_6H_5COH	COH	HCOH	HOCOH	*m*
C_6H_5COOH	COOH	HCOOH	HOCOOH	*m*
$C_6H_5SO_3H$	SO_3H	HSO_3H	$HOSO_3H$	*m*
$C_6H_5.CO.CH_3$	$CO.CH_3$	$HCOCH_3$	$HOCOCH_3$	*m*
$C_6H_5CH_2.COOH$	$CH_2.COOH$	$HCH_2.COOH$	$HOCH_2.COOH$	*o-p*

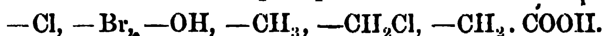
The authors point out expressly that the rule is no 'law', as the nature of the substituent has no obvious connection with the mechanism of the reaction.

Another way of formulating the rule is given by Armstrong,[1] who points out that ortho-para substitution takes place if an element is present in a group in which the atom attached to the nucleus is only linked to univalent atoms. Meta substitution, on the other hand, occurs if the attached atom is linked to multivalent atoms.

Vorländer has advanced a similar rule to the effect that in brominating, sulphonating, and nitrating a benzene substitution product C_6H_5E, the substituents E have a different influence according to whether the element in the side-chain is saturated or not. Chloro- and bromo-benzene, phenol, toluene, benzyl chloride, and phenylacetic acid give almost exclusively para and ortho substitution products, whereas from nitrobenzene, benzenesulphonic acid, benzaldehyde, benzonitrile, acetophenone, &c., mainly meta derivatives are formed. The groups which give rise to the entrance of nitro groups into the meta position are unsaturated:


$$-NO_2,\ -CN,\ -CHO,\ -COOH,\ -SO_3H.$$

Those which favour the ortho-para position are saturated:


$$-Cl,\ -Br,\ -OH,\ -CH_3,\ -CH_2Cl,\ -CH_2.COOH.$$

But none of these rules rigidly express the facts. It is difficult to draw a definite line between weakly and strongly negative atoms and groups as formulated by Hübner and Noelting. The Crum-Brown-Gibson rule does not explain the formation of *m*-nitroniline (NH_3 cannot be directly oxidised to NH_2OH) nor the production of ortho-para derivatives from toluene (CH_4 is directly oxidisable to methyl alcohol as Bone[2] has shown). Vorländer's rule falls short in

[1] *Trans. Chem. Soc.*, 1887, 51, 258. [2] *Trans. Chem. Soc.*, 1908, 93, 1575.

the case of unsaturated compounds such as cinnamic acid, ω-nitrostyrene, and azobenzene, which come within the ortho-para series. Moreover, there are cases where all three derivatives are formed; for example, when nitric acid acts on toluene. In addition to ortho and para, small quantities of meta-nitrotoluene are formed. The same occurs with the action of nitric acid on benzoic acid, in which the principal product is the meta compound; but ortho and para nitrobenzoic acids are also produced. Aniline, acetanilide, and benzanilide yield all three nitro derivatives and so does acetophenone. Another point to remember is that in cases where the three isomers have not been detected, one or other may have been overlooked owing to the experimental difficulties which attend the separation of a small quantity. But there are other exceptions in which the formation of the particular isomer and the relative quantity of it are determined by the conditions of the reaction. Acetanilide and fuming nitric acid give a mixture of ortho and para derivatives; in presence of strong sulphuric acid about 95 per cent. of para is produced; but if nitrated with nitrogen pentoxide in presence of acetic anhydride the product is almost exclusively the ortho compound. This is in agreement with the rule; but, on the other hand, if aniline is nitrated in presence of a large quantity of strong sulphuric acid, the main product is meta. Similar observations have been made with dimethylaniline, in which the presence of strong sulphuric acid gives rise to the meta derivative as principal product. A very curious result is obtained on introducing alkyl groups into toluene by the Friedel-Crafts reaction. Methyl enters mainly into the ortho position, propyl into the meta, butyl into the meta and para, and amyl probably into the para position. Holleman[1] does not regard this fact as opposed to the usual rule owing to the complicated nature of the reaction and the number of products formed. Blanksma[2] explains other exceptions by indirect substitution, in which the substituent first enters the side-chain and then passes into the nucleus. This applies to ortho-para substitution in the nitration of aniline. Direct or meta substitution is assumed to occur when sulphuric acid is present. This view cannot be generally applicable seeing that on nitrating or brominating bromobenzene indirect substitution cannot occur; nevertheless the products are ortho and para compounds.

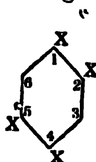
Although the general rules cited above in different forms are observed in the larger number of cases, it does not follow that the

[1] *Die direkte Einführung von Substituenten in den Benzolkern*, p. 196, A. F. Holleman. Veit, Leipzig, 1910.

[2] *Rec. des trav. chim. Pays Bas*, 1902, 21, 281; 1904, 23, 202.

proportion of ortho and para is retained under different conditions or on introducing different substituents. For example, in sulphonating phenol, the higher the temperature, the more para relatively to ortho compound is formed; in brominating toluene the para compound is the main product (60 per cent.), but in nitration it is the ortho compound which predominates (56 per cent.). Bromination of benzoic acid yields only the meta compound, but nitration yields all three nitro compounds. The character and amount of by-products are subject to considerable variation. If para is the main product, some ortho is usually formed, but little or no meta compound. If ortho is the main product, para is found with a little meta. If, finally, meta is the chief product, either ortho or para accompanies it, together with small quantities of the third isomer. None of these observations are without exceptions. Benzenesulphonic acid gives mainly the *m*-disulphonic acid (68 per cent.) and the rest is para free from ortho. Benzoic acid gives mainly *m*-sulphobenzoic acid, and again the para is the only by-product.

In regard to the rules which determine the entrance of substituents into higher substituted derivatives of benzene, it appears in the case of the halogens that when the first two hydrogen atoms have been replaced in the ortho, meta, or para positions, further substitution mainly follows in a direction which leads to a 1.2.4.5 derivative whatever the nature of the entrant group[1].



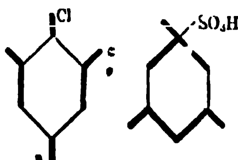
Theories of Benzene Substitution. Holleman in his treatise on 'Die Einführung von Substituenten in den Benzolkern' has discussed very fully the various theories which have been advanced at different times to explain the rules of substitution. Armstrong[2] adopts the view that addition precedes substitution; that in ortho-para substitution, the additive compound results from the union of the reacting molecule with the *carbon atom* to which the first radical is attached, whilst in meta substitution the additive compound is formed by the union of the reacting molecule with the *radical*, which usually contains an unsaturated group. In view of Bamberger's and

[1] Cohen and Dakin, *Trans. Chem. Soc.*, 1904, 85, 1274; Cohen and Hartley, *ibid.*, 1905, 87, 1360.

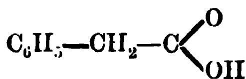
[2] *Trans. Chem. Soc.*, 1887, 51, 258.

Chattaway's observations on isomeric change where a group passes from side-chain to nucleus, yielding in the majority of cases ortho and para derivatives (Part II, p. 371), this view cannot be sustained.

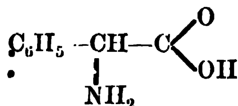
Flürscheim's Theory.[1] Flürscheim bases his view of substitution on Werner's theory of maximum disposable affinity which may be variously distributed according to the nature of the attached atoms as previously explained (p. 87). Elements which have a stronger affinity for carbon than hydrogen, such as chlorine, tervalent nitrogen in the amino group, oxygen in hydroxyl, &c., attach themselves more firmly than saturated atoms, such as nitrogen in the nitro group and in quinquevalent salts of amino compounds, carbon in carboxyl, and sulphur in the sulphonic acid group, &c. The former, by absorbing more of the affinity of nuclear carbon, lessen the amount which link the ortho carbon atoms, leaving a larger quantity available in the ortho and para positions, for the attachment of new substituents, whilst the latter, which are less firmly attached, will leave more available for attachment in the meta position. If the strength of affinity be denoted by thick and thin lines the distribution in the case of chlorine and the sulphonic group will appear as follows:



Such apparent anomalies as the entrance of the nitro group into the para position in phenylacetic acid and into the meta position in phenylglycine is explained in the same way by a different distribution of affinity.



Phenylacetic acid.



Phenylglycine.

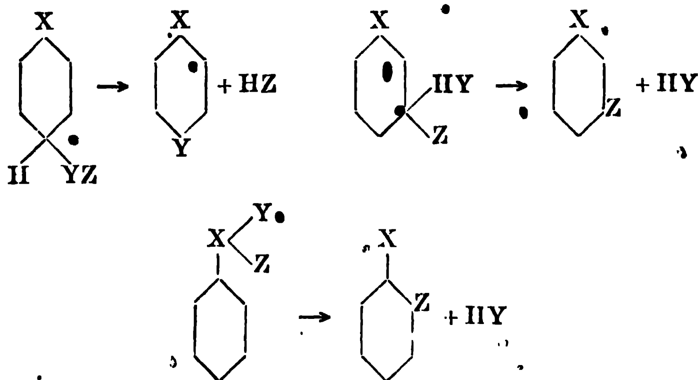
[1] *J. prakt. Chem.*, 1902, 66, 321; 1905, 71, 497.

But this explanation is scarcely satisfactory, for, as Obermiller points out, methyl, which is a saturated group and therefore weakly attached, produces ortho-para substitution in place of meta.

Without discussing in detail the other weak points in the theory, attention may at least be directed to one, namely the difficulty of explaining why ortho substitution in the first case should occur to the exclusion of meta, and why in the second case meta substitution should be produced to the exclusion of ortho, seeing that in both, the ortho and meta carbon atoms are joined by a weak and strong affinity, and have consequently a precisely equal affinity value. Moreover, as Holleman observes, the idea of a strong and weak attachment is purely relative; there is no definite line of demarcation, nor has any group a fixed and unalterable affinity value in relation to the nucleus. The nitro group in nitrobenzene is extremely stable compared with the fourth nitro group in tetranitrophenol, which water will remove in the form of nitrous acid.

Tschitschibabin's theory of substitution[1] bears a close resemblance to that of Flürscheim. It is based upon the principle already explained (p. 87) that unsaturated atoms mutually saturate one another up to a certain point, and that in consequence the carbon atoms in benzene are more saturated than the four in dihydrobenzene or the two in tetrahydrobenzene. Unsaturated groups, such as NH_2, by appropriating some of the affinity of the carbon atom of the ring leave less at the disposal of the latter, and consequently the ortho and also the para carbon atoms are less saturated. Nitrogen in the nitro group is, however, more saturated than in the amino group, and consequently the attached carbon atom is less saturated and has more affinity at the disposal of the ortho carbon atoms, which leaves less for the meta carbon atoms. The meta carbon atom is thereby less saturated. Aldehyde and carboxyl groups behave in the same way as the nitro group and for the same reasons. According to this view methyl should have a meta orienting effect, which is exactly the reverse of the fact. Tschitschibabin supposes that unsaturation is manifested by addition to the unsaturated atoms, and that it may occur either with nuclear carbon or hydrogen or with the atoms of a side-chain according to the character of the unsaturated atom or group and the nature of the addendum. He represents the process by the following schemes, in which X represents the substituent and YZ the addendum.

[1] *J. prakt. Chem.*, 1912, 86, 397.



In this way the ortho-para and the meta laws of substitution are explained, but the method of addition scarcely accords with modern views. The main difference between this and the former theory seems to be that whereas Flürscheim regards each group as appropriating a definite amount of chemical affinity under all circumstances, unsaturation, according to Tschitschibabin, is a variable quantity depending on environment.

It appears to us that the author confuses the notion of affinity as manifested by saturated and unsaturated atoms. Unsaturated atoms are, like oppositely charged conductors, at a higher potential than saturated atoms. Saturated atoms have a lower energy content and therefore exhibit a firmer union. This firmer union will affect both atoms alike, and the second will lose as much free affinity as the first and will therefore not gain by the transaction as Tschitschibabin seems to assume.

To explain the laws of substitution Obermiller[1] adopts the Claus diagonal formula for benzene, where each carbon atom of the nucleus is simultaneously linked to an ortho and para carbon atom which are thus similarly connected. He also regards substitution as a direct process not preceded by addition.

Substituents are divided into two classes: those which promote substitution and those which hinder it. The orienting effect of the first is directed towards the ortho and para positions, that of the second towards the meta position.

The division is not very clearly marked, and depends on the ease or difficulty with which the second and third member of the substituting group can be introduced into the nucleus. The meta-

[1] *Die orientierenden Einflüsse und der Benzolkern*, by J. Obermiller. J. A. Barth, Leipzig, 1909.

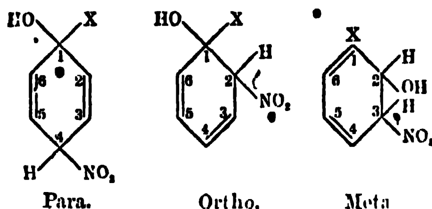
orienting influence of such groups as NO_2, SO_3H, and CO_2H is put down to steric hindrance due to the space occupied by the group. This effect may under certain circumstances be suppressed if the orienting influence of an ortho-para substituting group is present, as, for example, in the nitration of *m*-chloronitrobenzene when the second nitro group under the orienting influence of the chlorine atom enters the ortho position to the first group. Then, it may be asked, why does the nitro group frequently enter the ortho position rather than the para, where steric hindrance would have less effect?

Obermiller attempts to show that a low temperature and a slower rate of reaction overcome steric hindrance, and he cites the case of sulphonating phenol in the cold and in dilute solution, which yields the ortho-sulphonic acid mainly, whereas higher concentration and higher temperature give the para compound.

In other respects Obermiller adopts Werner's theory of valency, and his views, though somewhat differently expressed, bear a certain resemblance to those of Flürscheim. A weak affinity between the first substituent and nuclear carbon will strengthen that between the carbon atoms in the ortho and para position and weaken the affinity of the latter for hydrogen, which is more easily replaced in consequence. The closer the union between atoms, the greater will be their mutual influence, so that the ortho carbon atoms will be more affected by substitution than those in the para position; but steric hindrance may supervene and reverse the result. If steric hindrance prevents substitution in the para position as well, then meta substitution will occur.

The author, in short, lays down so many rules and assumes so many modifying circumstances that it is not surprising to find that the examples given fit in satisfactorily with one or other of the possible explanations.

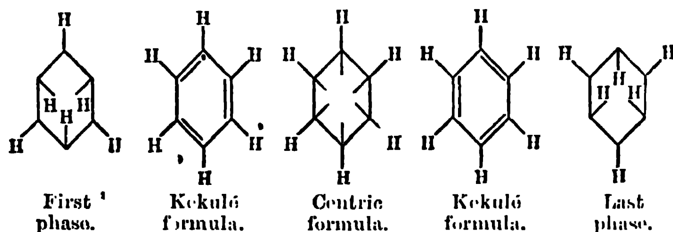
Holleman has suggested a less speculative and more reasonable explanation. Assuming Kekulé's formula for benzene, he supposes a radical X, being already present in the benzene nucleus, may promote or retard addition of the new substituent to the adjoining double bond. If it promotes addition, an ortho compound will result. Conjugation may cause addition in the para position, according to Thiele's theory (p. 133), in the same fashion. On the other hand, the addition in position 2 . 3 is uninfluenced by X, as it does not adjoin the double bond. In other words, addition is influenced by X in positions 1 . 2 and 1 . 6, but not in 2 . 3. The idea may be illustrated in the following manner. Let us suppose C_6H_5X to be nitrated; three additive compounds may be formed.



Para. Ortho. Meta

By subsequent removal of water a para, ortho, or meta nitro-compound is produced. If X accelerates the reaction, substitution follows the para-ortho rule, which may lead to the exclusion of any meta compound. If X has no such accelerating action, smaller or larger quantities of meta compound will be formed. Examples are afforded by the nitration of phenol and toluene. In the first case, where the rate of the reaction is high, ortho and para nitro-compounds only are formed; in the second, where the rate is slower, a certain amount of meta compound is produced. If X has a retarding effect, addition at 2.3 predominates. This view fits in very neatly with the observation that meta compounds are often accompanied by smaller quantities of ortho, for here the first addition occurs at 2.3 and then at 2.1, in which position 2 is common to both.

Collie,[1] by means of a model in which the carbon atoms with the attached hydrogen revolve, has illustrated the movement of the carbon atoms of benzene, whereby it is made to pass through various phases. These phases may be represented in a plane by means of figures in which the Kekulé and centric formulae recurrently appear, as representing certain states of the nucleus.

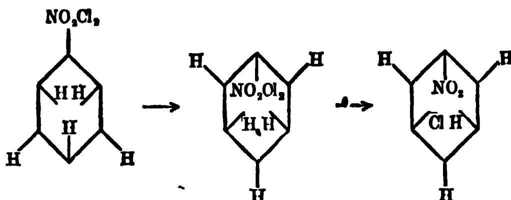


First phase. Kekulé formula. Centric formula. Kekulé formula. Last phase.

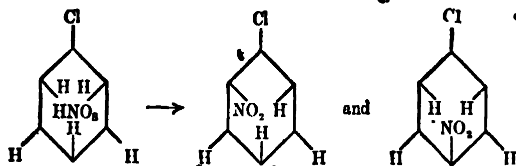
Supposing addition to the original unsaturated substituent to precede substitution, the orientation of the newly attached group will be dependent on the phase in which the addition occurs. If nitrobenzene were chlorinated, an additive compound $C_6H_5NO_2 . Cl_2$ will first be formed. In the first phase we may suppose the NO_2 group to occupy the position of one of the external hydrogen atoms, and, in

[1] *Trans. Chem. Soc.*, 1897, 71, 1013.

the last, that of one of the internal hydrogen atoms. In the latter position chlorine would be brought into close contact with the hydrogen atoms and substitution would take place in the meta position.

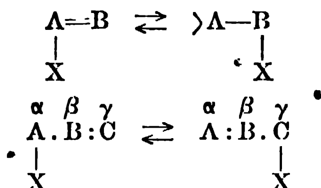


But, on the other hand, when nitric acid is allowed to react with chlorobenzene, no such additive compound would be formed, and the attraction of the three hydrogen atoms attached to the 2.4.6 carbon atoms might be just sufficient to determine its reaction with them and so produce ortho and para compounds.

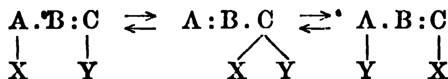


It must be confessed that the second explanation is not quite so convincing as the first.

Lapworth[1] bases his views on the dyad and triad type of isomeric change (Part II, p. 318) in which migration occurs from an α to a β atom with change of valency and from an α to a γ atom with change of linkage.



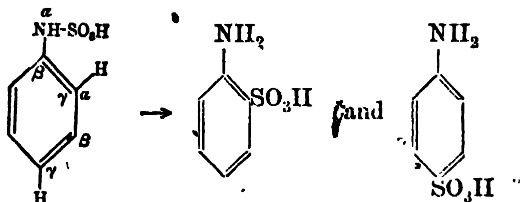
The idea has been extended by introducing a double migration, taking place successively in opposite directions, thus:



[1] *Trans. Chem. Soc.*, 1898, 73, 445; 1901, 79, 1265.

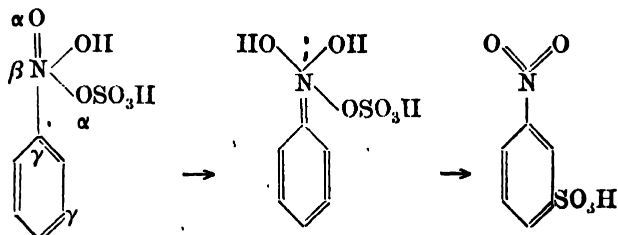
which may recur through a series of alternate singly and doubly linked atoms such as exist in benzene (Kekulé's formula).

The process is illustrated by isomeric change from side-chain to nucleus, as for example in the case of benzenesulphamic acid, when a sulphonic acid group wanders from nitrogen to the nucleus to form ortho and para anilinesulphonic acids (Part II, p. 371).



The sulphonic group wanders to the first γ atom in the ortho position and to the next γ carbon in the para position, whilst the hydrogen it displaces, wanders in the opposite direction.

The meta change is effected in the same way by migration in two directions; but owing to the unsaturation of the side-chain, the wandering group is farther removed from the nucleus. This may be illustrated in the case of the sulphonation of nitrobenzene.

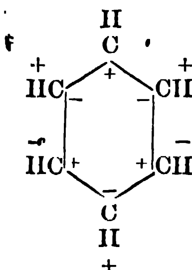


In this case the hydrogen migrates from the first γ position to the next γ position and thence to the oxygen of the nitro group, and the sulphonic groups make the reverse journey.

The conditions underlying the meta rule are formulated by Lapworth as follows: 'Where a substitution product is formed by isomeric change of a product of addition or substitution in the side-chain in which the substituting radical is separated from the benzene nucleus by *two intermediate atoms*, a meta substitution derivative must be produced or replacement of the side group by the new substituting radical will occur.'

Direct substitution in the nucleus is, according to Lapworth, determined by addition followed by cleavage as formulated by Armstrong and Holleman.

Electronic Theory of Substitution. H. S. Fry[1] has elaborated an interesting theory of substitution, which is based on the assumption that the atoms can either give or absorb electrons, or, in other words, can function both with positive and negative valencies, and that it is this opposition of electronic characters which bind the atoms in a molecule. Benzene is, therefore, represented by a ring of carbon atoms, linked alternately by positive and negative valencies to the positive and negative valencies of hydrogen.



This being assumed, it follows that in the formation of di-derivatives the dominant valency in the ortho and para position to the substituent group will be of the same sign, that in the meta position of opposite sign. Thus, a positive group will attach itself to a C − atom and a negative group to a C + atom. Similar atoms and groups should therefore substitute in the meta position and groups of different sign in the ortho and para positions. But in chlorination, the chlorine atoms form ortho and para di-derivatives. How is this explained? Every atom or group may react by virtue of its + or − valencies and may be + in one compound and − in another, or, indeed, both + and − in the same molecule, such, for instance, as the atoms in the chlorine molecule, or the two carboxyl groups in phthalic and terephthalic acids.

The theory, moreover, demands the existence of two mono-derivatives in which the substituent is attached to an electropositive or an electronegative carbon atom by an electropositive or negative valency.



The difficulty is overcome by assuming a form of tautomerism,

[1] *J. Amer. Chem. Soc.*, 1912, 34, 664; 1914, 36, 248, 262, 1035; 1915, 37, 855, 2368; 1916, 38, 1323; see also Vorländer, *Ber.*, 1919, 52, 263.

termed by the author *electronic*, in which isomeric equilibrium between the two forms is supposed to exist.

The same kind of electronic tautomerism may occur in other compounds, such as nitric acid.



The theory, in short, is so mobile, so adaptable and so ingeniously applied as to explain most of the facts of substitution as well as many reactions of aromatic compounds; but it cannot be discussed in greater detail.[1]

[1] The theory has, however, not escaped criticism: see Holleman, *J. Amer. Chem. Soc.*, 1914, 36, 2495.

CATALYTIC REACTIONS OF ORGANIC COMPOUNDS

Catalytic Reduction. Platinum and palladium in conjunction with hydrogen have been frequently used as reducing agents, and it has long been known that unsaturated hydrocarbons could be converted into paraffins and the oxides of nitrogen into ammonia by passing a mixture of the vapour or gas and hydrogen over the heated metal. The process is a typical catalytic or contact reaction, inasmuch as the metals greatly accelerate reduction without undergoing any fundamental change in composition or quantity, or bearing any molecular relation to the amount of material transformed.

It is not our intention to enter on a discussion of the mechanism of the process, about which there is some diversity of opinion, but merely to record its application in organic synthesis.

Bredig[1] was the first to obtain colloidal platinum by passing a current between electrodes of the metal below the surface of water. The metal appears to pass into solution, but the latter has none of the physical characters of a true solution, for it neither diffuses through animal membranes nor exhibits osmotic pressure. It is a pseudo or colloidal solution. He noticed its reducing action on nitrites and its effect in bringing about the union of hydrogen and oxygen.

In 1902[2] Paal found that colloidal solutions of metallic oxides and metals could be produced by adding alkali to the metallic salts in presence of the sodium salts of protalbinic and lysalbinic acid (hydrolytic products of protein), which act as 'protecting agents'. Later,[3] he prepared colloidal palladium, platinum, and indium by a similar method, using first hydrazine sulphate and afterwards free hydrogen as the reducing agent. The colloidal solutions in water and alcohol are very active, and in presence of hydrogen reduce such substances as oleic, cinnamic, maleic, and fumaric acids, to the saturated condition.

Wallach[4] has since carried out numerous experiments by Paal's palladium method and finds that ethylene compounds can be reduced, no matter where the ethylene bond occurs, and that the reduction can be effected with or without solvent and at the ordinary temperature, thus excluding the possibility of isomeric change. The reaction

[1] *Anorganische Fermente*, by G. Bredig. Leipzig, 1901.
[2] *Ber.*, 1902, 35, 2195, 2206, 2227.
[3] *Ber.*, 1905, 38, 1406, 2414; 1907, 40, 2209; 1908, 41, 805, 2273; 1909, 42, 3930.
[4] *Annalen*, 1911, 381, 52.

can be so regulated that the ketone group in $\alpha\beta$ unsaturated ketones is only slightly attacked.

In the meantime Fokin, who had been experimenting on electrolytic reduction with different metals as electrodes, found that those metals which are known to occlude hydrogen have the strongest reducing action. He subsequently observed that the solvent also plays a part, and that whilst one solvent will promote, another will prevent reduction.

Later[1] he introduced platinum and palladium black, and showed that oleic acid in ether solution in presence of these metals is reduced to stearic acid by passing in hydrogen at the ordinary temperature or in presence of nickel and cobalt at a high temperature. With colloidal platinum he succeeded in reducing a number of unsaturated organic acids and also acrolein, nitrobenzene, &c., but not the aromatic hydrocarbons.

Willstätter[2] then took up the subject and improved and simplified the process of reduction by using colloidal platinum, prepared according to Löw.[3] The method consists in reducing platinic chloride with formaldehyde in alkaline solution. The precipitate is then washed by decantation, until the platinum hydrosol begins to pass into solution, and filtered. The product, which is carefully excluded from the air, is very active, and is capable, in presence of hydrogen, of effecting the complete reduction, not only of unsaturated compounds, but also of benzene and naphthalene, which yield cyclohexane and decahydronaphthalene respectively, and other aromatic hydrocarbons and compounds such as phenol and benzoic acid, which give the hexahydro-derivatives. The colloidal metal can be used with various solvents. In the examples named, glacial acetic acid was added to the substance. The reducing activity is, however, dependent on the absence of certain substances, especially sulphur compounds, which appear to arrest the action completely.

Skita[4] has introduced palladious chloride in aqueous or alcohol-aqueous solution in presence of gum arabic as protective colloid. Under the action of hydrogen the palladium salt is reduced to the colloidal metallic condition and has effected the reduction of a number of organic compounds such as unsaturated ketones of the aliphatic and aromatic series.

d-Pulegone was reduced by hydrogen at two atmospheres pressure in presence of colloidal platinum to *d*-menthone; other reducing

[1] *Chem. Zentralbl.*, 1906, vol. ii, p. 758; 1907, vol. ii, p. 1324.
[2] *Ber.*, 1908, 41, 1475; 1912, 45, 1471. [3] *Ber.*, 1890, 23, 289.
[4] *Ber.*, 1909, 42, 1627; 1910, 43, 3393.

agents yield the laevo compound. In mesityloxide the ethylene group is reduced, but the ketone group remains intact, and the same is true of phorone; but by raising the pressure to five atmospheres the latter is converted into methyl isobutyl carbinol. Whilst Sabatier and Senderens' method (see below) leads to the rupture of the cyclopropane ring in thujene, Tschugaeff[1] found that platinum black and hydrogen at the ordinary temperature gave thujane. Rise of temperature also has an effect. Phenanthrene, for example, when reduced with palladium at the ordinary temperature yields tetrahydrophenanthrene, but at 160° the octahydride is formed. It will be seen from the foregoing examples that the action of finely divided platinum and palladium affords an effective and easily regulated reduction method of very extended application.

The Sabatier-Senderens Method.[2] The method consists in passing the vapour of the substance to be reduced, mixed with pure hydrogen, over finely divided nickel and certain other metals at an optimum temperature. The process originated in the observation that certain metals could be made to combine with nitrogen peroxide. An attempt to produce similar compounds with acetylene led the authors to pass the gas over finely divided metals (nickel, cobalt, iron, and platinum). with the result that it decomposed with incandescence. Further experiments carried out with ethylene at a temperature of 300° yielded a similar result; carbon was deposited, but the gas evolved proved to be ethane. Thus the saturated hydrocarbon was probably formed at the expense of the hydrogen of the unsaturated compound. This led the authors in 1899 to study the reducing action of finely divided metals, in conjunction with hydrogen, on a variety of organic compounds. Nickel proved to be the most active, but cobalt, iron, copper, and platinum were also found to effect reduction, the activity varying in different cases. Thus only nickel and cobalt can hydrogenate the aromatic nucleus.

Copper is less active than nickel, and in certain cases where the latter catalyst carries the reduction too far, metallic copper may be substituted. Very important factors are temperature and pressure, for it appears that these are probably reversible reactions,[3] in which the balance may shift under varying conditions. This will explain the existence of an optimum temperature for each reaction and the change of product with change of pressure. It is usual to

[1] *Compt. rend.*, 1910, 151, 1058.
[2] *Ber.*, 1911, 44, 1984. See also, *La Catalyse en Chimie Organique*, by P. Sabatier. Béranger, Paris, 1913.
[3] Ipatiew, *Ber.*, 1907, 40, 1270.

explain the reducing action of the metal by the formation of an unstable hydride, a view which accounts for the numerous cases of dehydrogenation, when the metal robs the compound of its hydrogen. But Ipatiew's discovery of the almost equally efficient action of nickel oxide, especially in presence of hydrogen under pressure, seems to point to the intermediate formation of water, which, according to Ipatiew, loses its hydrogen in an active form, regenerating the metallic oxide. The view receives some confirmation from Brunel's observation[1] that phenol is readily reduced to cyclohexanol by vaporising the phenol, previously liquefied, by the addition of water, that is, in presence of water vapour. The advantage of the Sabatier-Senderens over the preceding methods is the rapidity of the process and the large quantities of material which can be treated in a short time; its defect is the necessity of using rather high temperatures (150-200°) and the consequent difficulty of avoiding secondary reactions, polymerisation, isomeric change, and occasionally carbonisation.

The operation is conducted as follows: to obtain a large metallic surface, pieces of pumice are soaked in nickel nitrate solution and heated to convert the nitrate into oxide. The pumice is then introduced into a hard glass tube about two to three feet long and placed in a hot-air furnace. The oxide is reduced at a temperature of 320-350° in a current of hydrogen, carefully purified and freed, more especially, from traces of sulphur and halogen, which destroy the activity of the catalyst. The temperature is then regulated according to the nature of the substance to be reduced, which is introduced with the hydrogen in a steady stream. If gaseous, the two gases are admitted simultaneously; if liquid, the substance is dropped from a tap-funnel into the end of the tube; if solid, it is melted and vaporised in a current of hydrogen.

We will now consider briefly the effect of this method of reduction on various organic compounds. Among the earliest experiments conducted by Sabatier and Senderens was the reduction of carbon monoxide and dioxide. The former at 250° and the latter at 300° yield methane and water.

Olefines and Acetylenes. The interesting observation was made that when acetylene is reduced with excess of hydrogen at 200°, liquid condensation products are formed, consisting mainly of paraffins and closely resembling American petroleum. A second treatment of the material produced a certain quantity of hydro-aromatic hydrocarbons or *naphthenes* corresponding in character to

[1] *Compt. rend.*, 1904, 137, 1268.

the Caucasian product,' whilst if the reduction was conducted at 300° some of the hydrocarbons were converted into unsaturated cyclic hydrocarbons and the product resembled Galician petroleum in character.

The higher acetylenes behave differently. Diacetylene with copper as catalyst yields ethylbenzene and other substances in smaller quantity; nickel, on the other hand, yields ethylcyclohexane. The difference between the two catalysts is also brought out in the case of heptine C_7H_{12}, copper giving heptene C_7H_{14} and polymerisation products (di- and tri-heptene), and nickel effecting complete reduction to heptane. This difference in action of the catalysts is explained by Sabatier on the assumption that the metal, under varying conditions of temperature, is capable of forming different hydrides, and thus producing lower and higher states of hydrogenation.

Aromatic Hydrocarbons. Aromatic hydrocarbons (benzene and homologues) are readily converted into hexahydro-derivatives at 180°, and compounds with unsaturated side-chains yield the corresponding cycloparaffins. Styrene gives ethylcyclohexane, dipentene forms menthane, camphene yields dihydrocamphene, bornylene gives camphane, and pinene forms pinane. In the first experiments with naphthalene and acenaphthene, tetrahydro-derivatives were obtained. Since then, by working at lower temperatures, the decahydride of naphthalene, the tetra-, octa-, and tetradecahydrides of anthracene, the di-, tetra-, and dodecahydride of phenanthrene, and the decahydride of fluorene have been prepared.

Aldehydes and Ketones. Aliphatic aldehydes and ketones with nickel as catalyst are readily reduced to alcohols. By this method the formation of pinacones from ketones is avoided. Aromatic aldehydes such as benzaldehyde give benzene and carbon monoxide, whilst aromatic ketones give the corresponding hydrocarbons. The diketones, such as benzil and benzoin, also react smoothly, yielding dibenzil, and the quinones are easily converted into the corresponding quinol; in the case of benzoquinone the nucleus may also be reduced, and quinitol is formed.

Phenols. At a temperature of 215-230° the mono- and polyhydric phenols are reduced to cyclohexanols, and α and β naphthol form the decahydrides. If the temperature is too high they may lose hydrogen, giving the cycloketone. This elimination of hydrogen is exemplified in the case of the alcohols, which, with copper as catalyst, form aldehydes or ketones, and the latter in turn may lose carbon monoxide, and finally pass into hydrocarbons. An interesting example is that of allyl alcohol, which by loss of

hydrogen is partly converted into acrolein and partly by further reduction into propionaldehyde. At a lower temperature it is wholly converted into propyl alcohol. Benzyl alcohol yields benzaldehyde at 300° and benzene and carbon and carbon monoxide at 380°. Furyl alcohol is, however, reduced to methyl furfurane.

Unsaturated Ketones. In substances like mesityloxide, the ethylene, but not the ketone, group is reduced; unsaturated cyclic ketones, on the other hand, can be converted into cyclohexanols if the temperature is kept low and the speed regulated so that a large excess of hydrogen is present. In this way pulegone has been converted successively into pulegomenthone and pulegomenthol, carvone into dihydrocarveol, and thujone into thujol.

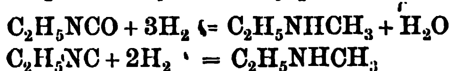
Unsaturated Acids and Esters of the aliphatic and aromatic series are readily reduced to the saturated condition. Acrylic acid is converted into propionic acid, oleic acid into stearic acid, and cinnamic acid into phenylpropionic acid. The esters, such as the unsaturated animal and vegetable oils, behave similarly. The process known as 'the hardening process' has become of great technical value. The liquid fish-oils become solid and the unpleasant smell is entirely removed on reduction.

Acids and Anhydrides. Acetic acid passed over heated copper at 400° breaks up into methane, carbon dioxide, and acetone; with zinc dust at 250° it gives acetone; propionic acid and the higher acids yield a mixture of aldehyde and ketone (propionaldehyde and diethylketone). Acetic anhydride with nickel breaks up into acetaldehyde and acetic acid. The nucleus in aromatic acids has not yet been reduced by this method. The effect on phthalic anhydride is to give phthalide.

Nitro-compounds are reduced to amines. Nitrobenzene passed over copper at 300° yields aniline, and other nitro-compounds behave similarly, whilst if nickel, the more powerful catalyst, is employed, the aniline breaks up into benzene and ammonia. Aliphatic nitro-compounds are less sensitive to nickel, and yield the amine at 150–180°.

Compounds such as oximes, cyanides, isocyanides, and isocyanic esters, which yield amines by other methods of reduction, are reduced in the same way by nickel and hydrogen. With aliphatic cyanides the product, as a rule, is not a single primary amine, but a mixture with the secondary and tertiary base, in which the secondary amine predominates. The latter is produced by union of two or more molecules of the primary amine, with elimination of ammonia. In the case of aromatic cyanides, cleavage into hydrocarbon and ammonia occurs. Phenyl cyanide gives toluene and ammonia.

Isocyanic esters and carbamines give secondary amines, but the reactions are complicated by secondary processes.



$$C_2H_5NCO + 3H_2 = C_2H_5NHCH_3 + H_2O$$
$$C_2H_5NC + 2H_2 = C_2H_5NHCH_3$$

Like the aliphatic cyanides, the aliphatic aldoximes give primary, secondary, and tertiary amines, in which the secondary amine predominates, whilst the cyclic oximes, such as acetophenonoxime, give in addition the unsaturated hydrocarbon. It is a remarkable fact that the esters of nitrous acid yield amines on reduction just like the isomeric nitroparaffins.

Aromatic Bases. The effect of temperature on the product of reduction is well illustrated in the case of aniline and other aromatic bases. Passed over nickel at a high temperature aniline breaks up into benzene and ammonia: at 190° it yields a mixture of cyclohexylamine, dicyclohexylamine $NH(C_6H_{11})_2$, and phenylcyclohexylamine $C_6H_5NHC_6H_{11}$; at 160–180° cyclohexylamine alone is formed, and the homologous amino compounds are readily reduced in the same way. Benzylamine, however, breaks up mainly into toluene and ammonia, with the formation of little of the cyclohexane derivative. The only satisfactory method of obtaining hexahydrobenzylamine is to utilise the Sabatier-Senderens synthesis of amines by passing a mixture of the alcohol and ammonia over heated thoria. Though attempts to reduce pyridine failed, the ring breaking and giving rise to amylamine, quinoline was converted into the tetrahydro-derivative by reduction of the pyridine nucleus, and pyrrole into pyrrolidine. Indole, curiously enough, breaks up and gives *o*-toluidine, and acridine forms $\alpha\beta$-dimethyl quinoline, in which one benzene ring is opened.

Halogen Compounds. The general effect of the process on halogen compounds is either to remove the halogen, which is eliminated as halogen acid, giving the unsaturated hydrocarbon, or simultaneously to replace it by hydrogen. The aliphatic mono-chloro compounds break up at 250° into hydrogen chloride and the olefine; 2.2 dichloropropane gives chloropropylene. Chloro- and bromo-benzene lose halogen and yield benzene.

Ipatiew's Method. The first experiments of Ipatiew were directed to the study of the pyrogenetic effect of different catalysts at high temperatures (600–800°), in the course of which he was able to show that a common result of such a process was the removal of hydrogen and also oxygen. In this connection, iron and zinc, that

is, easily oxidisable metals, were found to be peculiarly active. Alcohols passed through iron tubes, or tubes containing zinc, were converted into aldehydes and ketones, along with olefines formed by removal of water.

A variety of catalysts, including alumina and other metallic oxides, were examined, with interesting results, some of which corresponded closely with those obtained by the Sabatier-Senderens process. A novelty in the method was afforded by the use of hydrogen at high pressure, which was proved to accelerate the process. Ipatiew showed, for example, that ethylene in presence of alumina and hydrogen at a temperature of 400–450° and at a high pressure underwent polymerisation and reduction, yielding paraffins. Acetone, which undergoes no change in an iron tube at 400° with hydrogen at the ordinary pressure, is converted at 100 atmospheres to the extent of one-fourth into isopropyl alcohol.

A further development of the method was the action of the two oxides of nickel[1] on unsaturated compounds in presence of hydrogen at a pressure of 100–120 atmospheres. Benzene was completely reduced to cyclohexane at 250° in one and a half hours, with one-tenth of its weight of nickel oxide, the rate of reduction being therefore greater than with the metal. Other aromatic hydrocarbons, ketones and bases, phenols, terpenes, and quinoline were reduced more rapidly than in the Sabatier-Senderens process, and, in addition, the alkali salts of aromatic acids such as benzoic, phthalic, and β-naphthoic acids, which are unaffected by the free metal, yielded the hexahydro compounds in the first two cases and the tetrahydro and decahydro acids in the last. Copper oxide can in some cases replace nickel oxide with advantage.[2] The great difference in the rate of reduction seems to point to some other action than that of the metal and hydrogen. Ipatiew explains the process by supposing reduction of the nickel oxide to occur with the formation of water, which re-forms oxide and liberates active hydrogen.

Among reducing catalysts should be included metallic iron in its action on nitro-compounds, for it is well known that much less than the theoretical amount of hydrochloric acid is required for reduction. The process is explained by the alternate change of ferrous chloride into the magnetic oxide and reconversion into ferrous salt.

Dehydrogenation. It has already been pointed out that the above process, especially at higher temperatures, is reversible, and may

[1] *Ber.*, 1907, 40, 1270, 1281. [2] *Ber.*, 1909, 42, 2089.

lead to the elimination of hydrogen. Thus it has been shown that, with copper at 250–300°, the primary alcohols yield aldehydes, the secondary alcohols from ketones; tertiary alcohols, on the other hand, give olefines. Geraniol may be converted into citral, borneol into camphor, and menthol into menthone. Cyclohexanes pass into aromatic hydrocarbons. Cyclohexanols above 350° tend to revert to the phenol, the cyclohexylamines to the amino compounds; the dodecahydride of anthracene loses six atoms of hydrogen at 200° and eight atoms at 260°, reverting to anthracene at 310°. At 300° piperidine is converted into pyridine.

Paraffins also lose hydrogen, and apparently break down into unsaturated groups, CH_3, CH_2, CH, which reunite to form new saturated and unsaturated hydrocarbons. The results are much the same as those obtained by Berthelot by the thermal decomposition of the paraffins, but, in presence of a catalyst, are produced at a much lower temperature.

Dehydration. Whilst metallic catalysts are chiefly effective in adding or removing hydrogen, the metallic oxides, such as anhydrous alumina, thoria, the blue oxide of tungsten (W_2O_5), and, as Ipatiew has shown, aluminium phosphate and silicate, possess a dehydrating action.[1] At temperatures of 300° to 350° the alcohols (with the exception of methyl alcohol, which gives methyl ether) are converted into the corresponding olefines. Ethyl alcohol forms ethylene, and borneol gives menthene, &c. Two catalysts, such as copper and alumina or thoria, may thus produce essentially different reactions, for, with the metal, the alcohol loses hydrogen and yields aldehyde; but with the oxide it loses water and gives the olefine. According to Sabatier,[1] both reactions are determined by a labile union of the catalyst with the compound, which differ, however, in the nature of the products. The action of a dehydrating and a reducing catalyst may sometimes be combined, so that the olefine is first formed and then converted into the saturated hydrocarbon.[2] Carvomenthol has been converted in this way into menthane (Part III, p. 230).

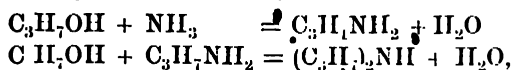
The dehydrating action of metallic oxides can also be accompanied by the addition of other groups, and Sabatier and Mailhe[3] have succeeded in preparing primary and secondary amines by passing a mixture of alcohol and ammonia over heated thoria at temperatures

[1] Ipatiew, *Ber.*, 1904, 37, 2986; Sabatier and Mailhe, *Ann. Chem. Phys.*, 1910, 20, 341.

[2] Sabatier and Murat, *Compt. rend.*, 1912, 155, 385; Ipatiew, *Ber.*, 1912, 45, 3205; *Ber.*, 1911, 44, 2000.

[3] *Comp. rend.*, 1911, 153, 160.

between 250° and 350°. Thus, propyl alcohol and ammonia give a mixture of propylamine and dipropylamine,



$$C_3H_7OH + NH_3 = C_3H_7NH_2 + H_2O$$
$$C_3H_7OH + C_3H_7NH_2 = (C_3H_7)_2NH + H_2O,$$

and benzyl alcohol yields benzylamine and dibenzylamine.

In the same way mercaptans can be prepared by the action of the catalyst on a mixture of alcohol vapour and hydrogen sulphide. Ethyl alcohol, for example, gives ethyl mercaptan.



$$C_2H_5OH + H_2S = C_2H_5SH + H_2O.$$

Esterification has also been effected in a similar fashion by passing the mixed vapours of alcohol or phenol and an organic acid over a metallic oxide. In this last reaction titanic oxide is more effective than thoria. With phenols and thoria as catalyst, diphenyl ethers are formed.[1]

Finally, thoria, alumina, lime, and other oxides at temperatures of 350° and 400° convert aliphatic acids and those aromatic acids with carboxyl in the side-chains, such as phenyl acetic and phenyl propionic acids, into ketones, whilst a combination of the acid and formic acid gives the aldehyde. In the latter case titanic oxide is the most effective catalyst.

References.

Ueber katalytische Reduktionen organischer Verbindungen, by Dr. A. Skita. Enke, Stuttgart, 1912.

Die Methoden der organischen Chemie, by Dr. B. Szelinski. Thieme, Leipzig, 1911.

Catalytic Oxidation. The earliest use of catalysts in oxidation is to be ascribed to H. Davy, who used platinum in effecting the union of hydrogen or marsh gas with oxygen, a phenomenon which was afterwards utilised by Döbereiner in his lamp. Here a jet of hydrogen was made to impinge upon a surface of platinum upon which oxygen was occluded; oxygen combined with the hydrogen, raising the platinum to incandescence and bringing about ignition of the jet. A later application of platinum as an oxidising agent was that by Hofmann to the preparation of formaldehyde, which Löw afterwards modified by replacing the platinum by copper. Colloidal platinum or copper was found to produce the same effect when air at the ordinary temperature was passed through methyl alcohol containing the metal in solution. Platinum black moistened with ethyl alcohol and exposed to air is converted into acetic acid, and

[1] Sabatier and Mailhe, *Comp. rend.*, 1912, 155, 260.

other organic compounds have been oxidised in a similar fashion. Cerous oxide, which, exposed to air in alkaline solution, passes into the trioxide, can bring about oxidation, though its use in organic chemistry is restricted. Vanadium in the form of oxide has been used along with chlorates in the production of aniline black from aniline, and the oxide of vanadium or ammonium vanadate has also been utilised in modifying the action and increasing the yield of oxalic acid by the action of nitric acid on sugar. But the most interesting of oxidising catalysts are iron in presence of hydrogen peroxide, and mercury or mercuric sulphate in presence of sulphuric acid.

The use of hydrogen peroxide in presence of a trace of ferrous salt was introduced and studied by Fenton[1] and has proved an invaluable reagent. Its action was first applied to the oxidation of tartaric acid, which is converted into dihydroxymaleic acid and later to that of the polyhydric alcohols, which are oxidised mainly to aldoses. Hydroxy acids are also readily attacked,[2] yielding aldehydic or ketonic acids.

Ruff[3] modified the method for preparing aldoses by oxidising the hydroxy acid obtained from one sugar, by means of Fenton's reagent, to the lower aldose of the series (Part III, p. 8).

It may be added that Dakin[4] has shown that normal saturated fatty acids and their phenyl derivatives may be oxidised to β-hydroxy and β-ketonic acids by the action of hydrogen peroxide on the acid without the addition of iron or its salts.

The first example of oxidation by the use of mercury in strong sulphuric acid was that of naphthalene, which at a temperature of about 275° is rapidly attacked and converted into phthalic acid. Anthraquinone is converted by the same process into hydroxyanthraquinone, and by protecting the hydroxyl groups by esterification with boric acid a hexahydroxyanthraquinone has been formed. The oxidation of aniline is greatly accelerated by the presence of mercuric sulphate at 275°. The use of persulphates in presence of silver peroxide and silver nitrate has also been applied as an energetic oxidising agent, which can convert benzene into quinone.[5]

The catalytic oxidation of enzymes or oxidases is discussed in Part III, chap. ii.

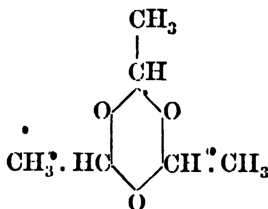
Catalytic Halogenation. To complete the series of catalytic

[1] *Trans. Chem. Soc.*, 1894, 65, 899; 1899, 75, 575.
[2] *Trans. Chem. Soc.*, 1900, 77, 69. [3] *Ber.*, 1898, 31, 1573.
[4] *Oxidations and Reductions in the Animal Body*, by H. D. Dakin. Monographs on Biochemistry: Longmans, Green, 1912.
[5] Kempf, *Ber.*, 1905, 38, 3963; Austin, *Trans. Chem. Soc.*, 1911, 99, 264.

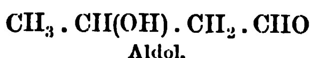
reactions of organic compounds, mention should be made of 'halogen carriers', which accelerate in a remarkable degree the process of chlorination and bromination. Among the more important are iron and its salts, the chlorides and bromides of antimony, molybdenum, aluminium, and phosphorus, sulphur and iodine.

Catalytic Condensation, such as the Friedel-Crafts reaction, is discussed under condensation (p. 195).

Polymerisation. The term polymerisation is clearly marked out from the process dealt with in a succeeding section on *condensation* by the nature of the product. A polymerisation product is one formed by the union of two or more molecules of the original compound in such a manner that depolymerisation, or cleavage into the original substance, is easily effected. The conversion of acetaldehyde C_2H_4O into paraldehyde $(C_2H_4O)_3$ is an example of polymerisation, for the latter on distillation with a small quantity of sulphuric acid yields the parent substance. Aldol $(C_2H_4O)_2$, on the other hand, cannot be broken up readily into acetaldehyde. The difference lies in the nature of the link between the molecules: in paraldehyde it is supposed to be effected by means of oxygen, in aldol by means of carbon.

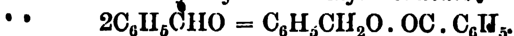


Paraldehyde.


$$CH_3 . CH(OH) . CH_2 . CHO$$
Aldol.

The property of undergoing polymerisation is peculiar to unsaturated compounds, from a natural tendency to saturate themselves. The formation of diisobutylene from isobutylene under the action of sulphuric acid or zinc chloride and that of benzene from acetylene must be included under condensation processes in accordance with the definition adopted above; but the conversion of aldehydes into the polymolecular paraldehydes, and the thio-aldehydes and -ketones into trithioaldehydes and trithioketones are examples of polymerisation. Polymerisation of the aldehydes is effected by small quantities of catalysts, such as mineral acids and certain metallic chlorides.

The change is also exhibited by aromatic aldehydes when acted upon by alkalis, but in this case intramolecular change occurs and an ester is formed. Benzaldehyde yields benzyl benzoate.


$$2C_6H_5CHO = C_6H_5CH_2O . OC . C_6H_5.$$

The only ketone which undergoes this change is acetone, which in presence of alkali yields diacetone alcohol $CH_3.CO.CH_2.C(OH).(CH_3)_2$, but breaks up on heating into acetone. The thio-aldehydes and -ketones polymerise so much more readily than the aldehydes that by acting on the aldehyde or ketone with hydrogen sulphide in presence of hydrochloric acid polymerisation occurs in process of formation.

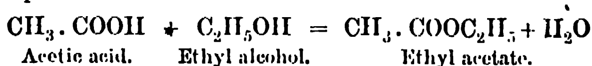
Polymerisation is very commonly observed among cyanogen compounds. Cyanogen itself yields paracyanogen $(CN)n$, hydrocyanic acid in alkaline solution deposits on standing a brown amorphous compound, which is probably aminomalonic nitrile $(CN)_2.CHNH_2$, whilst the alkyl cyanides yield di- and tri-molecular compounds. Liquid cyanogen chloride gives the solid tricyanogen chloride, cyanamide forms di- and tri-cyanamide (melamine). Cyanic acid and its esters also polymerise readily. Thiocyanic acid behaves like cyanic acid.

Light will sometimes effect polymerisation, as in the conversion of anthracene into dianthracene (see Part II, p. 149).

CHAIN AND RING FORMATION

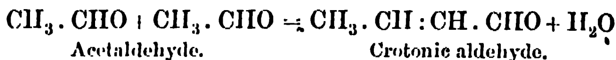
I. CONDENSATION. UNION OF CARBON AND CARBON

The terms *condensation* and *condensation product* imply a process and its result which have never been clearly defined, but which at the same time convey a distinct idea. Thus, the combination of ethyl alcohol and acetic acid to form an ester—a reaction in which water is separated—would not be termed condensation, yet the union of two molecules of acetaldehyde to form crotonic aldehyde, in which water is likewise removed, would be regarded as a typical example of such a process.



$$CH_3.COOH + C_2H_5OH = CH_3.COOC_2H_5 + H_2O$$

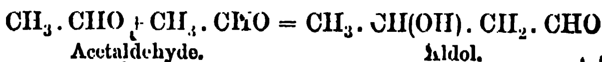
Acetic acid. Ethyl alcohol. Ethyl acetate.



$$CH_3.CHO + CH_3.CHO = CH_3.CH:CH.CHO + H_2O$$

Acetaldehyde. Crotonic aldehyde.

Again, all reactions, of which the conversion of aldehyde into aldol may be taken as the type, are termed *aldol condensations*, but in this case no water is separated.



$$CH_3.CHO + CH_3.CHO = CH_3.CH(OH).CH_2.CHO$$

Acetaldehyde. Aldol.

It is easy to draw a distinction between the formation of acetic ester from alcohol and acetic acid and that of crotonic aldehyde from acetaldehyde. In the first reaction the two molecules are linked in the new product by oxygen and are again readily separated by hydrolysis; but in the second reaction the new linkage is established between carbon atoms, and the product is consequently of a much more stable character. This might help us to a definition, were it not that in the third example no water is eliminated, although the new combination is effected between carbon atoms.

Although it is true that the formation of aldol is covered by the term *polymerisation* and should, strictly speaking, be included in this category, yet it is distinct from the process which gives rise to paraldehyde, a compound which, unlike aldol, is readily dissociated into the original aldehyde. In other words, the one is a reversible, the other is practically a non-reversible process.

As the formation of aldol is intimately linked with that of crotonic aldehyde, it would be illogical to draw distinctions between the two processes, and the term *aldol condensation* is therefore justified.

Condensation may then be defined as the union of two or more organic molecules or parts of the same molecule (with or without elimination of component elements) in which the new combination is effected between carbon atoms.

If this definition is accepted it will naturally embrace every kind of reaction in which new organic compounds are elaborated by the linking of carbon atoms. Used in this sense the word *condensation* can be conveniently applied to denote a certain section of the more comprehensive category of constructive chemical changes which are included in the term *synthesis*.

There is no intention of implying that the combination between carbon atoms is subject to different conditions from those obtaining among other elements. The union is, as a rule, more stable, but not necessarily so, and many reversible changes are known, in which carbon atoms part company as well as combine. We shall see presently that an almost equally stable union may be effected between carbon-nitrogen, carbon-oxygen, or carbon-sulphur, both in open chain and ring structures.

It must be recognised, therefore, that the distinction is an artificial one and merely convenient. Also, for convenience, it is desirable to distinguish between *external condensation*, in which two or more different molecules become linked together, and *internal condensation*, in which carbon atoms in the same molecule combine, leading to *ring formation*.

The process of condensation is connected with the early history of organic chemistry and was the outcome of the first systematic attempts at organic synthesis.

In the following pages it is intended to give a general survey of the principal condensation processes.

Nature of Condensation Processes. The examples of condensation (of which ring formation may be regarded as a special case) are so numerous and at the same time so varied in character that it would be impossible within the limits of a single chapter to enumerate them in anything like detail. Nevertheless, it is possible to lay down certain broad generalisations under which the different reactions may be grouped.

In the first place it will be observed that union between molecules or parts of a molecule is nearly always determined by unsaturation and by a consequent tendency for the unsaturated atoms to saturate themselves. On this basis condensation processes may be roughly divided into two groups: those in which the combining molecules are induced to unite by being rendered, as it were, artificially unsaturated as the result of withdrawing certain elements, and those which, being already unsaturated, combine either spontaneously or with the help of a reagent or catalyst.

To the first category belong those substances which, either by the action of heat or oxygen, lose hydrogen, resulting in the union of the residual groups. The linking up of compounds by the removal of halogen by the aid of a metal is illustrated by the processes of Fittig and Wurtz in chain formation, and by that of Freund and Perkin in the preparation of ring structures. Condensation effected by the separation of halogen acid through the action of catalysts is represented by the Friedel-Crafts method with aluminium and ferric chlorides, and by that of Ullmann with finely divided copper. The removal of carbon dioxide by heating barium or calcium salts of organic acids or their anhydrides and by electrolysis gives rise in the first case to ketones and in the second to paraffins and new homologous acids.

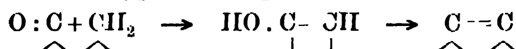
It is, however, to the second category, namely the union of unsaturated compounds, that the largest number of condensation processes belong. They may be divided broadly into those in which the combining molecules are both unsaturated, as in the union of acetylene with itself to form benzene, and those in which one molecule is saturated and the other not, as in Michael's, Reformatsky's, and Grignard's reactions (pp. 202–208).

But the process which has afforded the most varied and extended application is one which, for want of a better name, may be termed *intermolecular isomeric change*. In the chapter on isomeric change, Part II, chap. vi, the various types of change are enumerated and illustrated. These changes are brought about by the wandering of a hydrogen atom from one polyvalent atom to another in the molecule, accompanied by change of linkage. Suppose a similar process to take place between two polyvalent atoms belonging to different molecules, such a reaction would bring about mutual unsaturation, resulting in n... ion between them.

For example, the most common case of dynamic isomerism is the keto-enol change, which takes place when a hydrogen atom wanders from a carbon atom to a neighbouring oxygen atom.



Now if this change occurs between two molecules, one of which contains a CO group and the other a CH_2 group, as in the formation of aldol, we have a typical example of this kind of condensation,



a process which may or may not be followed by the removal of water and the production of an unsaturated compound.

Many examples of similar intermolecular isomeric changes occur, as for instance in Thorpe's reaction (p. 252), where the union of cyanogen derivatives with CH_2 groups takes place.

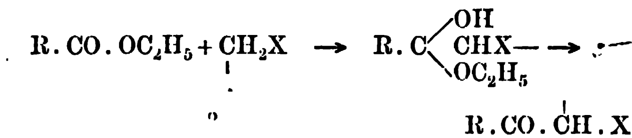


Michael's reaction might be included in the same category, corresponding to a shifting of the hydrogen atom within the molecule of an unsaturated hydrocarbon radical (see p. 202).



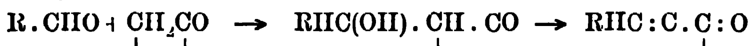
If we consider the various types of isomeric change and the large number of compounds which they include, the wide range and variety of the condensation products to which the above process may be applied will be easily realised. At the same time it is restricted in its application, being dependent mainly on the vicinity of certain active (usually negative) groups, and, to a smaller degree, on the nature of the condensing agent. A paraffin, although it contains numerous CH_2 groups, does not undergo condensation of the aldol type with an aldehyde or ketone under any conditions. Formaldehyde,

the most reactive of these substances, which readily condenses with aromatic hydrocarbons, cannot be induced to combine with methane or its homologues unless a negative group such as CO, CN, NO_2 replaces at least one atom of hydrogen in the paraffin. The acetoacetic ester synthesis, in which two esters unite under the influence of metallic sodium or sodium ethoxide, is undoubtedly an additive process, although resulting in the separation of a molecule of alcohol. It may be given the following general form :



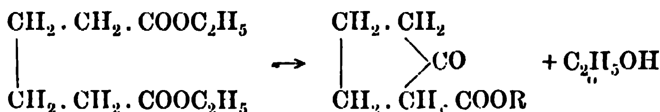
The X in the formula stands for an acid radical which may be not only an ester group, but an aldehyde, ketone, cyanogen, nitro or unsaturated ester or ketone group, HC : CH . CO.

The aldol and benzoin condensations and Claisen reactions consist in the union of two molecules of aldehyde, frequently followed by the removal of water and formation of an unsaturated aldehyde, as already explained.



Here again the CO group in the CH_2 . CO complex may be replaced by carboxyl (Perkin's reaction), carbethoxyl, and the other negative groups mentioned above, whilst the aldehyde may be substituted by a ketone (Claisen's and Knoevenagel's reactions, pp. 238, 241).

Ring Formation. Nearly all the above reactions may become intramolecular if the necessary grouping is present, and in such cases ring formation follows. But the process in some cases is subject to certain limitations, which depend on the number of atoms composing the ring. The acetoacetic ester synthesis, for example, may be applied intramolecularly to adipic, pimelic, and suberic esters, but not to glutaric or succinic esters.



In other words, it is possible to form a 5, 6, and 7 carbon ring, but not one of three or four carbon atoms.

Baeyer's Strain Theory. The commonest type of cyclic compounds occurring in nature are those consisting of 5 or 6 atoms.

and, as a matter of experience, they are of all ring structures the most readily produced, and the most stable under the action of heat and reagents.

An ingenious and very plausible explanation has been advanced by Baeyer under the name of the Strain (*Spannung*) Theory, which is based upon stereochemical considerations. Supposing the four valencies of carbon to be directed towards the solid angles of a regular tetrahedron, they will make angles of 109° 28′ with one another. Any distortion or deviation of these valency directions will lead, according to the theory, to a condition of strain which will make itself evident by loss of stability, and the greater the strain the greater the instability.

Baeyer regards an olefine as the first member of the cyclic series, in which the normal position of the two bonds uniting the carbon atoms is assumed to be bent so as to form straight parallel links between the atoms. The amount of distortion can be estimated, for each bond is bent inwards through half the total angle which the two make with one another, $\frac{1}{2}(109° 28′) = 54° 44′$; in a cyclopropane derivative, in which the carbon atoms may be supposed to make an equilateral triangle, the amount of displacement will be $\frac{1}{2}(109° 28′ - 60°) = 24° 44′$. The amount of deviation from the normal is given in the following table :

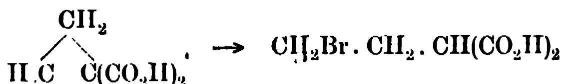
Cycloethane (Ethylene)	$\frac{1}{2}(109° 28′)$	54° 44′
Cyclopropane	$\frac{1}{2}(109° 28′ - 60°)$	24° 44′
Cyclobutane	$\frac{1}{2}(109° 28′ - 90°)$	9° 44′
Cyclopentane	$\frac{1}{2}(109° 28′ - 108°)$	0° 44′
Cyclohexane	$\frac{1}{2}(109° 28′ - 120°)$	−5° 16′
Cycloheptane	$\frac{1}{2}(109° 28′ - 128° 34′)$	−9° 33′
Cyclooctane	$\frac{1}{2}(109° 28′ - 135°)$	−12° 46′

It will be seen that the condition of greatest strain will occur in the olefine, that of least strain in the cyclopentanes, and then in the cyclohexanes. In the last three the strain will be outwards instead of inwards.

Stability of Ring Structures. We will now consider briefly to what extent the experimental facts harmonise with Baeyer's theory. It should be stated at the outset that the theory has reference to cycloparaffins and their derivatives, but does not necessarily include aromatic compounds or heterocyclic systems, which will be considered separately; for the unsaturated nature of the aromatic nucleus and the presence of other atoms than carbon in the ring may, and probably do, affect the stability of the system. No great importance need therefore be attached to an observation such as that of Markownikoff, who found that a cyclopentane derivative on

bromination in presence of aluminium bromide is converted into a brominated benzene.

At the same time it is a significant fact that among heterocyclic, as well as homocyclic compounds, 5 and 6 atom rings are not only most easily prepared, but of commonest occurrence among natural products derived from animal and plant organisms. Although there are certain facts not in harmony with the theory, which, as Aschan[1] says, cannot be elevated to the position of a law, like the theory of Van 't Hoff and Le Bel, it nevertheless presents a rough picture of molecular mechanics, which has had the effect of stimulating inquiry and enriching the science with fruitful results. In studying the stability of the cycloparaffins and their derivatives, it is important to remember that this property varies with the nature of the radicals attached to the cyclic carbon atoms. Kötz,[2] who made a careful study of the subject, found that the stability of the cyclopropane ring is diminished by the introduction of alkyl groups and increased by that of carboxyl, and Buchner[3] has shown that the latter effect is further enhanced when the carboxyl groups are attached to different carbon atoms. For example, cyclopropane 1,1, dicarboxylic acid undergoes disruption in contact with hydrobromic acid in the cold,



whereas the 1.2 dicarboxylic acid is not affected even when boiled with the concentrated reagent. The effect of carboxyl on the stability of 3- and 4-carbon rings is, in short, so great that frequently more depends on the nature and position of the radicals than on the number of carbon atoms in the ring.[4]

We will consider first the stability of the different cycloparaffins towards reagents, then the facility with which they are formed, and finally their conversion into one another.

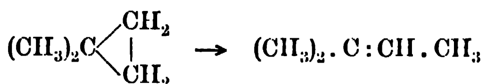
Action of Reagents. Taking ethylene as representing the first member of the cyclic series, it is characterised by the ease with which it unites with halogens, halogen acids, strong sulphuric acid, and undergoes oxidation with permanganate. These properties, which are manifested in the hydrocarbon itself, may be modified to a greater or less extent, as we have seen (p. 116), in certain of its

[1] *Chemie der alicyklischen Verbindungen*, by O. Aschan. Vieweg, Brunswick, 1905.

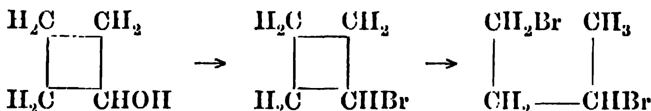
[2] *J. prakt. Chem.*, 1903, 68, 156. [3] *Annalen*, 1895, 284, 198.

[4] Perkin and Simonsen, *Trans. Chem. Soc.*, 1907, 91, 817; Perkin and Goldsworthy, *Trans. Chem. Soc.*, 1914, 105, 2665; Kenner, *Trans. Chem. Soc.*, 1914, 105, 2685.

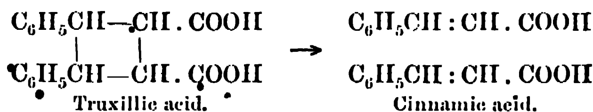
derivatives. Cyclopropane combines with bromine in sunlight, though not so readily as benzene, to form trimethylene bromide; it unites quite readily with hydrobromic and hydriodic acids, giving normal propyl bromide and iodide, and with sulphuric acid, forming propyl hydrogen sulphate, which on heating with water is converted into *n*-propyl alcohol. In all these reactions it resembles ethylene, but differs in its indifference towards permanganate, which is without action. Cyclopropane is decomposed above 550° (or, as Ipatiew[1] found, at 100° by passing it through a tube filled with iron filings) and gives propylene. Dimethylcyclopropane is completely converted into trimethylethylene when passed over alumina at 350°.



Cyclobutane is inert towards halogens, halogen acids, sulphuric acid, and permanganate, and is unaffected by heat. Cyclobutanol is, however, converted by hydrobromic acid into 1.3 dibromobutane,[2]



and truxillic acid breaks up on heating into two molecules of cinnamic acid:



but in these cases the stability of the ring is modified by the presence of radicals.

In cyclopentane and cyclohexane and their derivatives ring cleavage is never effected by any of the reagents mentioned above, unless the ring is already weakened by the attachment of oxygen to carbon in the form of ketone groups.

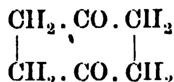
Increasing stability of the ring up to five and six atoms of carbon is also proved by the heat of combustion, which is discussed at greater length in a later chapter (Part II, p. 68). It is there shown that the heat of combustion decreases from ethylene to cyclohexane, indicating increasing stability or decreasing energy content. Stohmann and Kleber compared the mean difference between the heats of combustion of the cycloparaffins and the paraffins, allowing for the two

[1] *Ber.*, 1902, 35, 1063; 1903, 36, 2014.
[2] Perkin, *Trans. Chem. Soc.*, 1894, 65, 951.

additional hydrogen atoms in the open-chain compound, the results of which are given in calories in column I, whilst the mean loss of energy is given in column II.

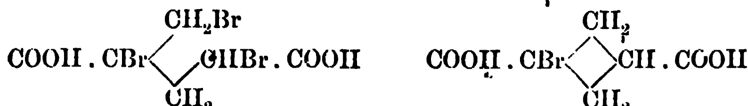
	I cals.	II cals.
Cycloethane (ethylene)	33.1	35.9
Cyclopropane	37.1	31.9
Cyclobutane	39.9	29.1
Cyclopentane	16.1	52.9
Cyclohexane	14.3	54.7

Evidence of Ring Formation. It is well known that certain general reactions which lead to the formation of 5 and 6 atom rings fail when it is attempted to produce smaller or larger ring structures. The acetoacetic ester synthesis when applied to glutaric ester is a case in point (p. 178). Similarly calcium adipate, pimelate, and suberate yield respectively cyclopentanone, cyclohexanone, and cycloheptanone (p. 226), whereas calcium succinate gives in place of cyclopropanone a cyclic diketone of the double formula[1]



Perkin[2] found, from his method of using sodium malonic ester and a dibromoparaffin in ring formation (p. 192), that whilst the 5-carbon ring is produced almost quantitatively, the 4-carbon ring is found in smaller quantity and a still smaller yield of the 3-carbon ring is obtained. The 6-carbon ring also gave a poorer yield than the 5-carbon ring, whilst the 7-carbon ring was prepared under considerable difficulty.

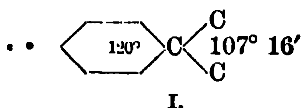
Another interesting fact of the same order is the action of zinc on $\alpha\beta\delta$-tribromobutane dicarboxylic acid, which might form either a cyclopropane or cyclobutane derivative.[3] It is exclusively the second reaction which occurs.



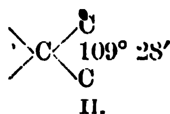
An observation pointing in the same direction was made by Thorpe and Campbell[4] in the case of cyclopropane and cyclobutane cyanacetic esters, the former, under the action of sodiocyanacetic ester, giving an open chain condensation product, whereas the cyclobutane derivative combined, but preserved the ring intact.

[1] Feist, *Ber.*, 1895, 28, 731. [2] *Ber.*, 1902, 35, 2105.
[3] Perkin and Simonsen, *Trans. Chem. Soc.*, 1909, 95, 1169.
[4] *Trans. Chem. Soc.*, 1910, 97, 2418.

Experiments have been carried out by Thorpe, Beesley, and Ingold [1] to ascertain which of the two types of compound, I or II, would more easily form a cyclopropane ring.



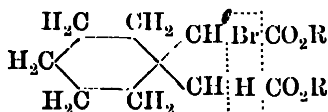
I.

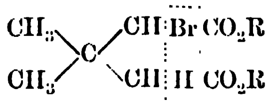


II.

For if cyclohexane represents a regular hexagon, the endocyclic angles must be 120°, thereby changing the angle which the exocyclic carbon atoms make with the cyclic carbon from 109° 28′ (the normal angle) to 107° 16′. It follows, therefore, from Baeyer's theory that type I, where the carbon atoms are in closer proximity, should yield a three-carbon ring more readily than type II.

The two substances submitted to experiment were α-bromocyclohexane diacetic ester representing type I and α-bromo-ββ-dimethyl glutaric ester corresponding to type II.

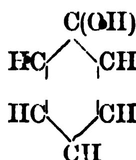


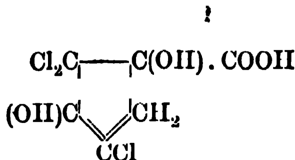


The result clearly indicated that by removal of hydrogen bromide type I gave a more easily formed and more stable ring than type II.

Transformation of Ring Systems. One of the most interesting features of this problem is the evidence of stability furnished by the change of one ring system into another.

The work of Zincke and Hantzsch on the action of chlorine in alkaline solution on the phenols and other aromatic compounds has afforded numerous examples of the change of a 6-carbon ring into a 5-carbon ring. We may take the case of ordinary phenol which passes into a derivative of cyclopentane.



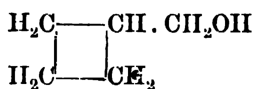


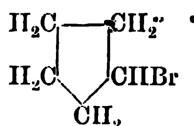
Most of the other phenols behave in a similar fashion.[2] Wreden found that when benzene is reduced with hydriodic acid at 300°, it yields a hydrocarbon C_6H_{12}, which was first mistaken for cyclohexane, but its low boiling-point (70°) and its conversion into

[1] *Trans. Chem. Soc.*, 1915, 107, 1080.

[2] Meyer-Jacobson, *Lehrbuch der organischen Chemie*, vol. ii, part i, p. 82.

a mixture of glutaric, succinic, and acetic acids on oxidation left no doubt as to its identity with methylcyclopentane. Zelinsky also found that cyclohexanol, on reduction with hydriodic acid, gives a mixture of cyclohexane and methylcyclopentane. Aschan has since shown that cyclohexane changes to methylcyclopentane on simply heating in a closed tube with or without aluminium chloride. A reaction of the same kind is the conversion of suberyl iodide with hydriodic acid into methylcyclohexane and dimethylcyclopentane. Cyclobutylcarbinol and hydrogen bromide give cyclopentyl bromide.[1]



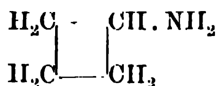


Cyclobutylcarbinol. Cyclopentyl bromide.

In all these cases it may be taken that there is a change from the less to the more stable ring system.

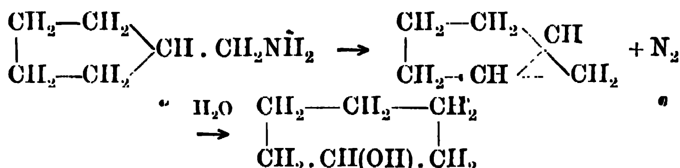
Examples of the conversion of a 4-carbon ring to a 5-carbon ring are also furnished by pinene, which with hydrogen chloride passes readily into bornyl chloride, that is, from a bridged ring of 4 carbon atoms to one of 5 (see Part III, p. 219).

Certain exceptions must be recorded. Demjanow[2] found that by the action of nitrous acid, cyclobutylmethylamine is converted into cyclopentanol and by loss of water into cyclopentene. This reaction is, however, capable of converting a larger into a smaller system; for when cyclobutylamine is acted upon with nitrous acid, it yields a mixture of cyclobutanol and cyclopropylcarbinol.



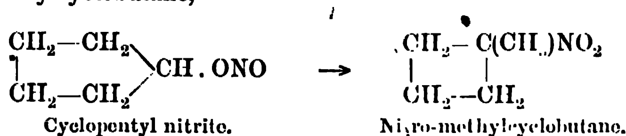

Cyclopentylmethylamine gives with the same reagent cyclohexyl alcohol and cyclohexylmethylamine is converted into suberyl alcohol.

Wallach[3] explains the latter reactions by assuming the formation of an intermediate labile double-ring structure, which undergoes hydrolysis.



[1] Demjanow, *Chem. Soc. Abstr.*, 1910, 1, 838.
[2] *Chem. Soc. Abstr.*, 1903, 1, 403. [3] *Annalen*, 1907, 353, 331.

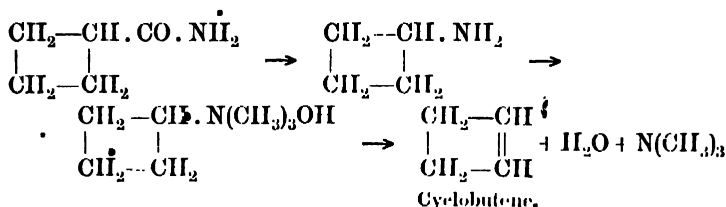
Further, cyclopentyl nitrite, obtained by the action of silver nitrite on cyclopentyl iodide, yields, when treated with concentrated alkali, nitro-methylcyclobutane,[1]



from which it appears that cyclic compounds without side-chains pass into smaller rings with side-chains, whereas, if a side-chain is present in the original compound, the tendency is to form a larger ring.

In concluding this account of the conditions which determine the formation of the cycloparaffins, a description of the preparation of some of the simpler members of the group is appended.

The preparation of cyclopropane is described under Wurtz's method (p. 188), and was first effected by Freund. Like propane it is a gas. Methylcyclobutane was prepared by Perkin by the method above referred to; cyclobutane itself was obtained by Willstätter[2] by a method which he has successfully applied to the preparation of other cycloparaffins and which requires a little explanation. Cyclobutanecarboxylic acid, obtained from the dicarboxylic acid (prepared by Perkin), by heating is converted into the amide, which by Hofmann's reaction is transformed into the amine. From this, on methylation, cyclobutyltetramethylammonium hydroxide is formed, which on distillation loses trimethylamine and water and yields cyclobutene. The latter is finally reduced by the Sabatier-Senderens process (p. 164).

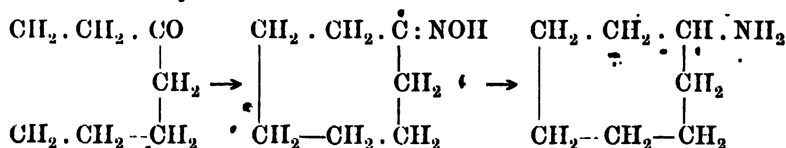


Cyclopentane was first prepared by Wislicenus from cyclopentanone by reduction (p. 189). Cyclohexane was obtained in the same way from cyclohexanone by Zelinsky,[3] from cyclohexadione by Baeyer (p. 225), and by Perkin from hexamethylenedibromide

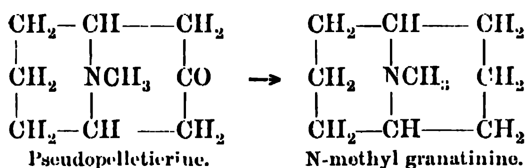
[1] Rosanoff, *Chem. Soc. Abstr.*, 1915, i. 657.
[2] *Ber.*, 1905, 38, 1992.
[3] *Ber.*, 1895, 28, 780; 1901, 34, 2799.

(p. 192). It has also been obtained by the direct reduction of benzene (p. 163).

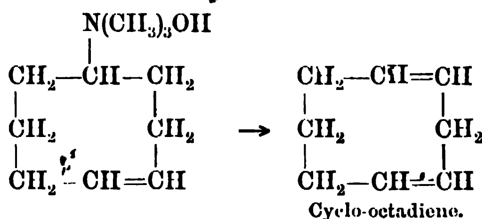
Cycloheptane has been prepared by Markownikow[1] from suberic acid by Wislicenus' method, that is, by conversion into the ketone and reduction in the same manner as cyclopentane (p. 200). It has also been prepared from the ketone by conversion into the oxime and reduction to the amine by Willstätter,[2] who used the method applied in the case of cyclobutane.



Cyclo-octane has also been prepared by Willstätter[3] and Veraguth from pseudopelletierine by exhaustive methylation. Pseudopelletierine is an alkaloid found in pomegranate and is related to tropinone (Part III, p. 318). On reduction it yields N-methyl granatinine.



On methylation the bridge is broken and the following substance is formed, which on distillation loses water and trimethylamine and gives α-cyclo-octadiene.



This compound rapidly polymerises, but if converted into the dihydrobromide and hydrobromic acid removed with quinoline, a second more stable β-cyclo-octadiene is formed, which on reduction by the Sabatier-Senderens method gives cyclo-octane. Cyclononane has been prepared by Zelinsky[4] by Wislicenus' method from sebacic acid by distillation of the calcium salt and conversion into the cyclic ketone.

[1] *J. Russ. phys. Chem. Soc.*, 1893, **25**, 364.
[2] *Ber.*, 1908, **41**, 148.
[3] *Ber.*, 1907, **40**, 957.
[4] *Ber.*, 1907, **40**, 3277.

The following are the boiling points of the cycloparaffins and the corresponding olefines and paraffins :

Number of carbon atoms.	Olefine.	Paraffin.	Cyclo-paraffin
3	−48°	−35°	−45°
4	−5°	+12°	+1°
5	+40°	49°	36°
6	69°	81°	69°
7	95°	117°	98°
8	122°	146°	126°
9		171°	150°

REFERENCE.

Chemie der alicyklischen Verbindungen, by O. Aschan. Vieweg, Brunswick, 1905.

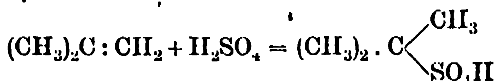
Group 1. Condensation by separation of Elements.

Removal of Hydrogen. Under the action of heat and certain reagents condensation may take place with loss of hydrogen. Benzene passed through a hot tube is converted into diphenyl.

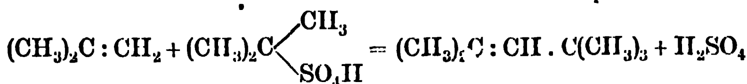


$$2C_6H_6 = C_6H_5 . C_6H_5 + H_2.$$

Diphenylmethane yields fluorene, and stilbene is converted into phenanthrene. Isobutylene when heated with strong sulphuric acid yields a mixture of isomeric diisobutylenes; but this reaction is no doubt brought about by the alternate addition and removal of sulphuric acid rather than by the direct elimination of hydrogen.[1]

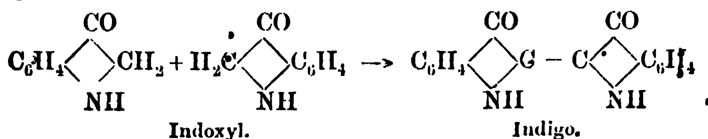


$$(CH_3)_2C : CH_2 + H_2SO_4 = (CH_3)_2 . C \begin{cases} CH_3 \\ SO_4H \end{cases}$$



$$(CH_3)_2C : CH_2 + (CH_3)_2C \begin{cases} CH_3 \\ SO_4H \end{cases} = (CH_3)_2C : CH . C(CH_3)_3 + H_2SO_4$$

Hydrogen may also be removed and condensation induced by the action of oxidising agents. An illustration of the process is afforded by the linking of two indoxyl (thioindoxyl or bromindoxyl) groups in alkaline solution in presence of atmospheric oxygen, to form indigo and its derivatives,



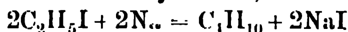
Indoxyl. Indigo.

[1] Butlerow, *Annalen*, 1877, 189, 65.

The use of oxidising agents is usually more effective. Dimethylaniline, for example, when oxidised with sulphuric acid and lead peroxide is converted into tetramethyldiaminodiphenyl and the formation of magenta from a mixture of *o*- and *p*-toluidine and aniline may be cited as a similar case of condensation.

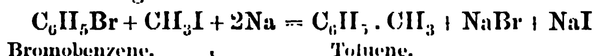
Removal of Halogens. It was in the pursuit of the free radicals that Frankland first used potassium and the alkyl cyanides, which in 1849 he replaced by zinc and the alkyl iodides (p. 35).[1] This inquiry resulted in two discoveries of the highest importance—the synthesis of the paraffins and the production of the first organometallic compounds. The method devised by Frankland of using a metal to remove the halogen from an organic halogen compound, so as to effect a union between the residual parts of the molecules, has undergone a wide extension.

The Method of Wurtz. In 1855 Wurtz[2] introduced sodium in place of zinc for preparing different paraffins from the alkyl iodides, as, for example, butane from ethyl iodide,



$$2C_2H_5I + 2Na = C_4H_{10} + 2NaI$$

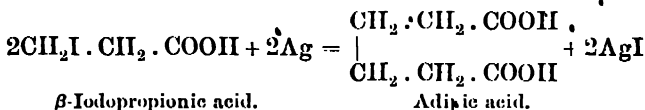
and the same method was applied by Fittig[3] in 1863 to the preparation of the homologues of benzene:



$$C_6H_5Br + CH_3I + 2Na = C_6H_5 . CH_3 + NaBr + NaI$$

Bromobenzene. Toluene.

In 1868 Wislicenus[4] employed finely divided metallic silver in the synthesis of dibasic from monobasic acids.

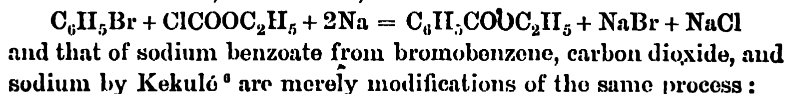


$$2CH_2I . CH_2 . COOH + 2Ag = \begin{array}{l} CH_2 . CH_2 . COOH \\ | \\ CH_2 . CH_2 . COOH \end{array} + 2AgI$$

β-Iodopropionic acid. Adipic acid.

Finely divided copper, although occasionally used in place of silver, has only received extended application as a condensing agent in recent years[5] (see p. 199).

The formation of benzoic ester by Wurtz from bromobenzene, chloroformic ester, and sodium,



$$C_6H_5Br + ClCOOC_2H_5 + 2Na = C_6H_5COOC_2H_5 + NaBr + NaCl$$

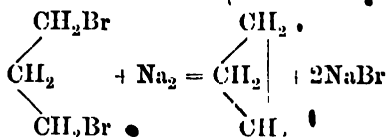
and that of sodium benzoate from bromobenzene, carbon dioxide, and sodium by Kekulé[6] are merely modifications of the same process:



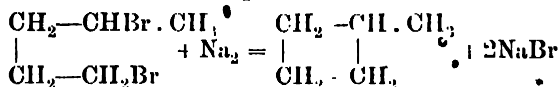
$$C_6H_5Br + CO_2 + 2Na = C_6H_5COONa + NaBr$$

[1] *Phil. Trans.*, 1852, 142, 417; *Annalen*, 1853, 85, 329.
[2] *Annalen*, 1855, 96, 365.
[3] *Annalen*, 1863, 131, 304.
[4] *Annalen*, 1868, 149, 221; *Ber.*, 1869, 2, 720.
[5] Ullmann, *Ber.*, 1903, 36, 2383; 1904, 37, 853; *Annalen*, 1904, 332, 38; *Ber.*, 1905, 38, 729, 2120, 2211.
[6] *Annalen*, 1866, 137, 180.

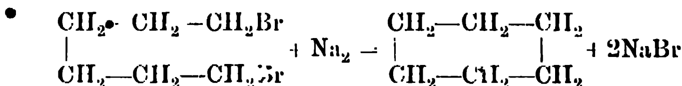
The same principle has been applied by Freund[1] to the production of ring compounds by internal condensation in the synthesis of cyclopropane from trimethylene bromide and sodium or zinc,



and by Perkin, jun.,[2] and his collaborators in the synthesis of methyl cyclobutane from 1.4 dibromopentane,



and cyclohexane from hexamethylene dibromide,



Removal of Sodium by Halogens and Halogen Compounds. The Method of Wislicenus. The discovery of a series of organic compounds of the nature of 1.3 diketones, such as acetylacetone, acetoacetic ester, malonic ester, acetone dicarboxylic ester, and similarly constituted compounds, such as cyanacetic ester, benzyl cyanide, desoxybenzoin, &c., which form sodium compounds by the replacement of hydrogen by sodium, gave a new impulse to the study of organic synthesis. The further discovery by Conrad[3] that in the preparation of the sodium compounds metallic sodium or dry sodium ethoxide could be replaced by an alcoholic solution of sodium ethoxide added greatly to the convenience of the method. We are not concerned for the moment either with the structure of the sodium compounds, which has been discussed under tautomerism (Part II, chap. vi), nor with the mechanism of the formation of the compounds themselves, which finds a place under the acetoacetic ester synthesis (p. 222). Our attention at present will be directed to the description of a few of the more important synthetic operations in which the sodium compounds have been utilised.

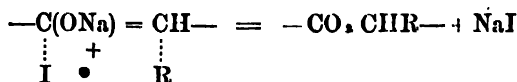
Before doing so, it will clear the ground in connection with this and many other reactions to be subsequently described, if the conditions which determine the mobility of a hydrogen atom in a hydro-

[1] *Monatsh.*, 1882, 3, 625.
[2] *Trans. Chem. Soc.*, 1888, 53, 201; 1891, 65, 599.
[3] *Annalen*, 1880, 240, 127.

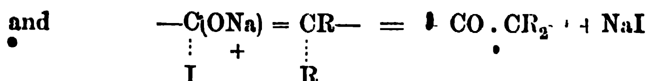
carbon (CH_2) group are more carefully defined. As a rule the proximity of a negative group produces this effect; but in a varying degree, depending partly on the strength of the negative group, partly on that of the metal or metallic compound used. Acetone, in which one CO group is present, does not react with sodium ethoxide, though it forms a sodium compound with metallic sodium. A phenyl group enhances the mobility and acetophenone $C_6H_5 . CO . CH_3$ is more reactive, but here again sodium ethoxide is without action. If, however, sodamide be substituted and the product acted on with an alkyl iodide, the three hydrogen atoms of the methyl group may be replaced successively by alkyl groups.[1] The presence of a phenyl, cyanogen, carbethoxyl, or an ethylene group produces much the same effect as a carboxyl group. A nitro group may, on the other hand, determine the formation of a sodium compound. In all these cases the presence of a second negative group will produce the required mobility of the hydrogen atom, which seems necessary to produce a sodium compound. Consequently, reactivity is manifested (1) by the 1.3 diketones with the group $CO . CH_2 . CO$, which includes esters like malonic ester, (2) by compounds with the group $CO . CH_2 . CN$, such as cyanacetic ester, (3) by those with the group $CO . CH_2 . C_6H_5$, like phenylacetic ester and desoxybenzoin, (4) by substances such as $C_6H_5 . CH_2 . CN$, and (5) finally by compounds which contain an ethylene linkage $CO . CH_2 . CH : CH$, such as glutaconic ester $C_2H_5OOC . CH_2 . CH : CH . COOC_2H_5$, which can be methylated by the action of sodium ethoxide and methyl iodide, yielding a mono- and dimethyl derivative.[3]

We will now turn to the various reactions in which the formation of a metallic derivative enables the above group of compounds to participate. If to an alcoholic solution of these compounds containing the equivalent of one atom of sodium, an alkyl iodide is added and the liquid boiled until neutral, sodium iodide separates and the alkyl derivative is formed. The process may usually be repeated by adding a second atomic equivalent of sodium in alcohol and a second molecule of alkyl iodide, when the dialkyl derivative is obtained. If these sodium compounds possess, as they admittedly do, the enolic structure, the action of the alkyl iodide must be represented by some such general schemes as the following, in which addition precedes substitution (see p. 124).[3]

[1] Haller and Bauer, *Compt. rend.*, 1909, 148, 70.
[2] Henrich, *Ber.*, 1898, 31, 2103.
[3] Michael, *J. prakt. Chem.*, 1892, 46, 194; 1899, 60, 316; *Annalen*, 1891, 266, 67, 113; 1892, 270, 330; Thorpe, *Trans. Chem. Soc.*, 1900, 77, 923.



and



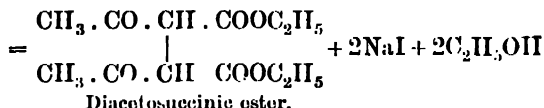
It will be seen that the negative iodine unites with the positive sodium and the positive radical with the carbon which forms part of a negative group.[1] It should be noted in passing that by substituting pyridine for sodium ethoxide as condensing agent, the alkyl attaches itself to the oxygen and the isomeric enolic form is produced.

The use of these methods for synthesising acids and ketones from acetoacetic ester, and acids from malonic and cyanacetic ester, belongs to the elementary facts of organic chemistry and need not be discussed in detail.

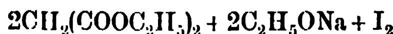
If, in place of an alkyl iodide, iodine is added to the alcoholic solution of the sodium compounds, polybasic acids may be obtained from acetoacetic ester and malonic ester as follows:[2]



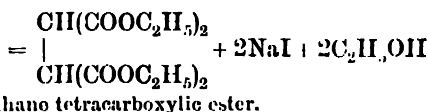
Acetoacetic ester.



Diacetosuccinic ester.



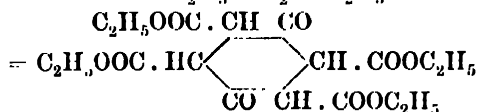
Malonic ester.



Ethane tetracarboxylic ester.

This method[3] has been used in the preparation of a cyclohexane derivative by acting upon the disodium compound of acetone dicarboxylic ester with iodine.

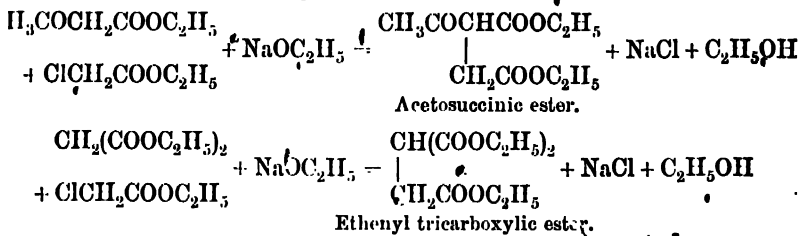




Again, if a halogen derivative of a fatty ester like chloracetic ester

[1] This view is embodied in Michael's 'positive-negative' theory (see p. 114).
[2] Harrow, *Annalen*, 1880, 201, 142; Bischoff and Rach, *Ber.*, 1884, 17, 2781.
[3] v. Pechmann, *Ber.*, 1897, 30, 2569.

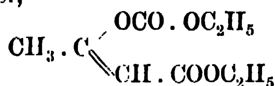
is allowed to interact, a variety of polybasic acids may be prepared, which the following examples will serve to illustrate:[1]



Acetosuccinic ester.

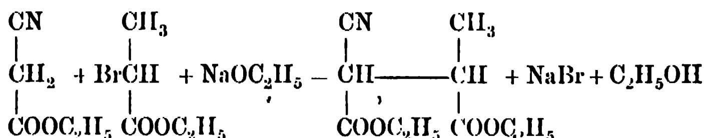
Ethenyl tricarboxylic ester.

Chloroformic ester is an exception to the general rule in producing mainly the enolic ester,

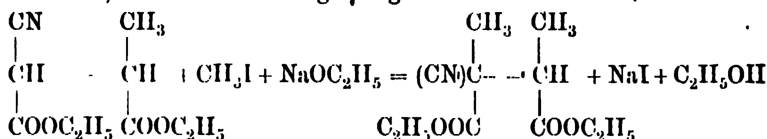


Cyanacetic ester behaves in precisely the same way as malonic ester. To take one example, symmetrical dimethylsuccinic ester has been prepared as follows:[2]

By the combined action of cyanacetic ester, α-bromopropionic ester, and sodium ethoxide, cyanomethyl succinic ester is first obtained.



The substance is then boiled up with methyl iodide and sodium ethoxide, when the following change occurs:



Finally, the product is hydrolysed with hydrochloric acid, whereby the cyanogen group is converted into carboxyl and removed as carbon dioxide, yielding symmetrical dimethylsuccinic acid.

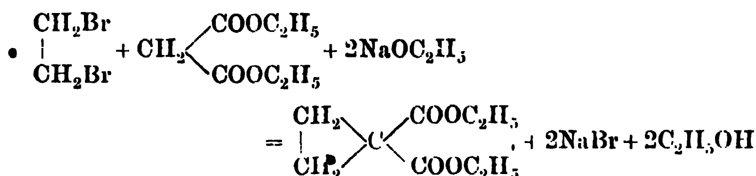
The Synthesis of Cyclic Compounds (Perkin's Method). The formation of sodium compounds of 1.3 diketones, more especially of malonic and acetoacetic ester, has found a further important application in the production of cyclic compounds.[3] The subject can only be briefly outlined.

[1] Bischoff and Rach, *Annalen*, 1882, **214**, 38; 1886, **234**, 36; Conrad, *Annalen*, 1877, **188**, 218.

[2] Bone and Sprankling, *Trans. Chem. Soc.*, 1899, **75**, 839.

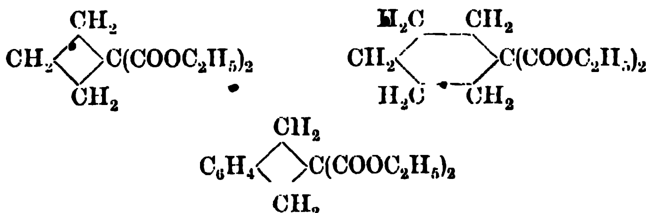
[3] W. H. Perkin, jun., *Ber.*, 1902, **35**, 2091.

Ethylene bromide and sodium malonic ester give cyclopropane dicarboxylic ester.



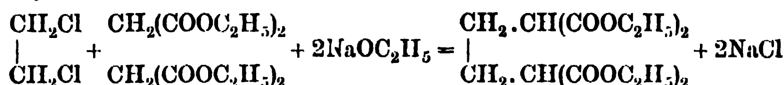
The product when hydrolysed gives the dibasic acid, and, on heating, the corresponding monobasic acid.

In a precisely similar fashion trimethylene bromide, pentamethylene bromide, and *o*-xylylene bromide have been converted into cyclic compounds having the following structure:

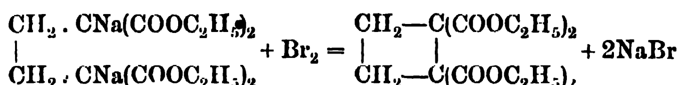


From each of these the corresponding di- and mono-basic acids have been prepared.

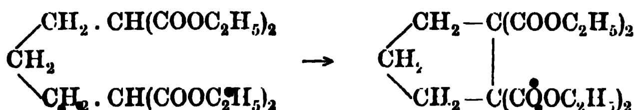
Cyclic formation may also be effected in the following way: ethylene chloride, malonic ester, and sodium ethoxide yield, in addition to the cyclopropane compound already described, an open-chain ester.



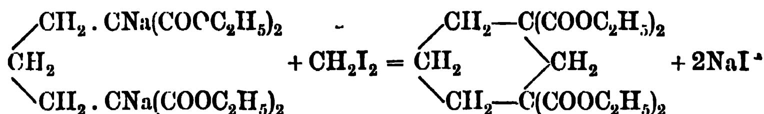
If this butane tetracarboxylic ester is converted into the disodium compound and then treated with bromine or iodine, ring formation occurs.



In place of ethylene chloride trimethylene bromide may be used when cyclopentane tetracarboxylic ester is formed.



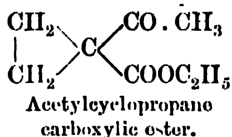
Furthermore, by introducing methylene iodide in place of iodine in the last reaction, a cyclohexane derivative is obtained.



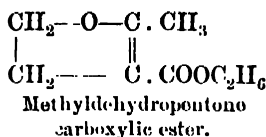
Each of these tetracarboxylic esters may be converted into dicarboxylic acids by the usual process of hydrolysis and heating.

The above series of reactions when applied to acetoacetic ester, benzoylacetic ester, or acetone dicarboxylic ester gives a somewhat different result.

Ethylene bromide, acetoacetic ester, and sodium ethoxide yield not only acetylcyclopropane carboxylic ester, in which the action proceeds normally as in the case of malonic ester, but the enolic form of acetoacetic ester also comes into play, giving an inner ether, methyldehydropentone carboxylic ester.

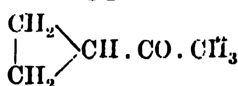


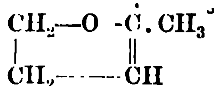
Acetylcyclopropane carboxylic ester.



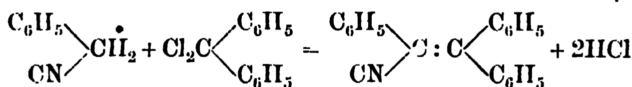
Methyldehydropentone carboxylic ester.

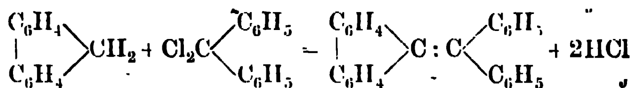
In the case of trimethylene bromide, the second reaction proceeds to the complete exclusion of the first. On hydrolysis of the above esters, the acid, which is formed, loses carbon dioxide on heating and gives the following products:



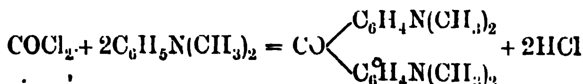


Removal of Hydrogen Chloride. Many halogen compounds condense directly with other organic compounds on heating, with the elimination of hydrogen chloride. Benzyl cyanide and fluorene unite in this way with benzophenone dichloride:

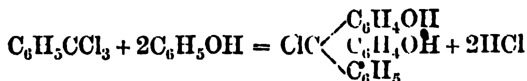




Carbonyl chloride combines with dimethylaniline,

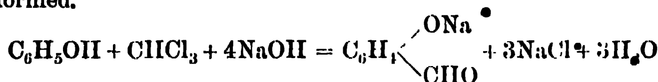


and benzotrichloride forms a derivative of triphenylmethane with phenols.

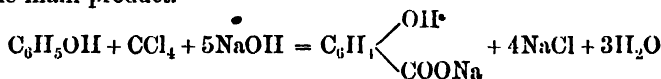


Reimer-Tiemann Reaction.[1] In this reaction chloroform and carbon tetrachloride unite with phenols in presence of caustic soda solution or sodium ethoxide, giving hydroxyaldehydes in the first case and hydroxy acids in the second.

With ordinary phenol a mixture of *o*- and *p*-hydroxybenzaldehyde are formed.

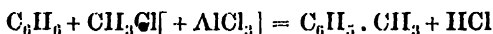


With ordinary phenol and carbon tetrachloride, the *p*-compound is the main product.

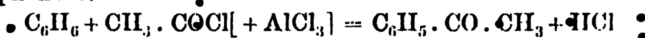


The Friedel-Crafts Reaction. The reaction, discovered in 1877 by Friedel and Crafts,[2] in which anhydrous aluminium or ferric chloride are the active agents, has had an extraordinarily wide and varied application in organic synthesis. It is connected more particularly with the union of aromatic hydrocarbons and their derivatives with a variety of other organic compounds, such as alkyl halides, acid chlorides, &c. Hydroxyl and amino groups, if present in the nucleus, must be protected by converting the former into an ether and the latter into an acetyl derivative. Nitro compounds do not react.

Hydrocarbons can be obtained by combining an alkyl halide, e.g. methyl chloride, with benzene in presence of anhydrous aluminium chloride, when a vigorous evolution of hydrogen chloride occurs and toluene is formed.



Ketones can be prepared in the same way by using an aromatic hydrocarbon and an acid chloride. Benzene and acetyl chloride give acetophenone.

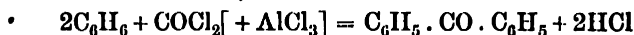


According to V. Meyer[3] a second acetyl group can only be intro

[1] *Ber.*, 1876, 9, 1285.
[2] *Compt. rend.*, 1877, 84, 1392; *Ann. Chim. Phys.*, 1884, (6), 1, 506.
[3] *Ber.*, 1896, 29, 847, 1413, 2568.

duced if both lie between two ortho methyl groups as in mesitylene. If, in place of acetyl chloride, chloracetyl chloride is substituted, a third radical is readily introduced.[1]

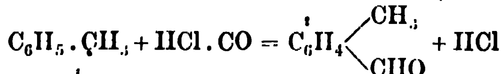
Carbonyl chloride and benzene react in a similar manner.



$$2C_6H_6 + COCl_2[+ AlCl_3] = C_6H_5 . CO . C_6H_5 + 2HCl$$

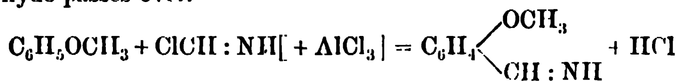
Aldehydes have been obtained by uniting an aromatic hydrocarbon with a mixture of carbon monoxide and hydrogen chloride in presence of dry cuprous chloride and aluminium chloride.[2]

p-Tolylaldehyde has been prepared from toluene.

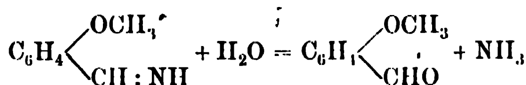


$$C_6H_5 . CH_3 + HCl . CO = C_6H_4\begin{cases}CH_3\\CHO\end{cases} + HCl$$

A better method was subsequently found for obtaining the aldehydes of phenols and phenol-ethers by the use of the compound of hydrogen chloride and hydrogen cyanide. $HCN . HCl$ is prepared *in situ* by passing the mixed gases into the phenol ether and aluminium chloride. The imino-compound, which is formed, is acidified with hydrochloric acid and distilled in steam, when the aldehyde passes over.

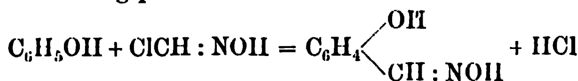


$$C_6H_5OCH_3 + ClCH : NH[+ AlCl_3] = C_6H_4\begin{cases}OCH_3\\CH : NH\end{cases} + HCl$$



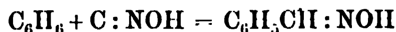
$$C_6H_4\begin{cases}OCH_3\\CH : NH\end{cases} + H_2O = C_6H_4\begin{cases}OCH_3\\CHO\end{cases} + NH_3$$

Aldoximes are obtained by combining chloroformaldoxime with phenols[3] or aromatic hydrocarbons with mercury fulminate,[4] the first reaction taking place as follows:



$$C_6H_5OH + ClCH : NOH = C_6H_4\begin{cases}OH\\CH : NOH\end{cases} + HCl$$

and the second, in presence of a little aluminium hydrate, according to the following equation, which gives a yield of seventy per cent. of syn-aldoxime:



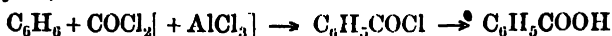
$$C_6H_6 + C : NOH = C_6H_5CH : NOH$$

From both compounds aldehydes are readily obtained by hydrolysis.

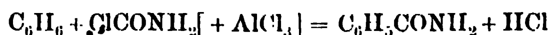
Acids can be prepared either by the action of carbonyl chloride in

[1] *Ber.*, 1901, **34**, 1826.
[2] Gattermann and Koch, *Ber.*, 1897, **30**, 1622; *Annalen*, 1906, **347**, 347; 1907, **357**, 313.
[3] Scholl, *Ber.*, 1901, **34**, 1441.
[4] Scholl, *Ber.*, 1899, **32**, 3493; 1903, **36**, 10, 322.

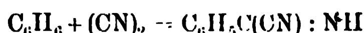
the proportion required to give the acid chloride, which is then hydrolysed,



or by the action of chloroformamide, which is obtained by heating cyanuric acid in a current of hydrogen chloride, the vapours being then passed directly into the hydrocarbon containing aluminium chloride. The amide of the acid is finally hydrolysed.

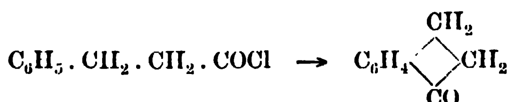


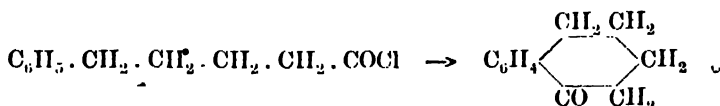
Vorländer[1] has succeeded in condensing benzene with cyanogen



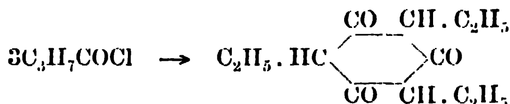
which yields benzoyl cyanide on hydrolysis.

Aluminium chloride has also been used by Kipping[2] for effecting internal condensation in the case of phenylpropionyl chloride and phenylvaleryl chloride, in which ring formation occurs, the first giving rise to hydrindone, and the second to benzocyclo-heptanone.[3]

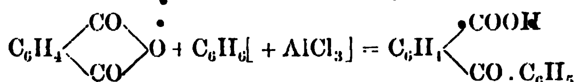




Combes,[4] by acting on butyryl chloride with aluminium chloride, obtained a cyclohexane derivative.



In most of the foregoing reactions a halogen compound is used in conjunction with the hydrocarbon, and hydrogen chloride is evolved. But aluminium chloride can also act as a condensing agent by virtue of its dehydrating action, and in other ways. Thus, phthalic anhydride and benzene condense to *o*-benzoylbenzoic acid :[5]



[1] *Ber.*, 1911, 44, 2455. [2] *Trans. Chem. Soc.*, 1894, 65, 484.
[3] Kipping and Hall, *Proc. Chem. Soc.*, 1899, 15, 173.
[4] *Compt. rend.*, 1894, 118, 1336. [5] Heller and Schülke, *Ber.*, 1908, 41, 3627.

Phenylcarbimide combines to form benzanilide,



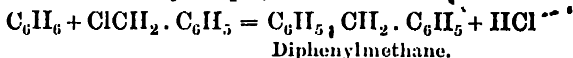
$$C_6H_6 + CO:NC_6H_5[+AlCl_3] = C_6H_5 . CO . NH . C_6H_5$$

and sulphur dioxide produces benzene sulphinic acid.



$$C_6H_6 + SO_2[+AlCl_3] = C_6H_5 . SO_2H$$

Reactions similar to the above can also be carried out with anhydrous ferric chloride, and in some cases, as in the union of benzene with benzyl chloride, a minute quantity of zinc or copper in powder, or the aluminium-mercury couple, will effect condensation.



$$C_6H_6 + ClCH_2 . C_6H_5 = C_6H_5 . CH_2 . C_6H_5 + HCl$$

Diphenylmethane.

It should be pointed out that the aluminium chloride occasionally reverses the process of condensation, for Jacobsen[1] has shown that if hexamethylbenzene, to which a small quantity of aluminium chloride is added, is heated in a current of hydrogen chloride, methyl groups are successively detached, with the formation of penta-, tetra-, &c., methylbenzenes, and, finally, benzene. Another interesting fact connected with the reaction is the transference of methyl groups from one hydrocarbon to another under the influence of this reagent. Anschütz and Immendorff[2] obtained from toluene both benzene and *m*- and *p*-xylene.

Various theories have been advanced to explain these curious changes. Friedel and Crafts assumed the formation of an intermediate compound, $C_6H_5 . Al_2Cl_5$, which unites with the alkyl halide, regenerating aluminium chloride.



$$C_6H_5Al_2Cl_5 + C_2H_5Cl = C_6H_5 . C_2H_5 + Al_2Cl_6$$

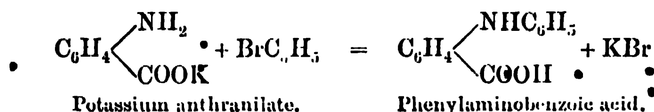
This would represent the chloride as a true catalyst, in which a small quantity would be sufficient to bring about the union of an indefinite amount of the reacting materials. In practice, this is not usually the case, for it is found that the amount of product increases approximately with the quantity of reagent. As Steele[3] has pointed out, this fact does not necessarily preclude the action of the aluminium chloride as a catalyst, provided it can be shown that it forms a stable compound with the product. The observations of Gustavson[4] and others seem to point in this direction.

Gustavson[5] isolated a number of definite compounds of aluminium chloride and hydrocarbon, and aluminium chloride, alkyl halide and hydrocarbon (possessing such formulae as $Al_2Cl_6 . 6C_6H_6$, and with ethyl chloride $Al_2Cl_6 . C_6H_3(C_2H_5)_3 . 6C_6H_6$), which appear to act as catalysts.

[1] *Ber.*, 1885, 18, 339. [2] *Ber.*, 1885, 18, 657. [3] *Trans. Chem. Soc.*, 1903, 83, 1490.
[4] *Compt. rend.*, 1903, 136, 1065; 1905, 140, 940; J. W. Walker and Spencer, *Trans. Chem. Soc.*, 1904, 85, 1106. [5] *Ber.*, 1878, 11, 2151.

More recently Menschutkin, Pfeiffer, and others have succeeded in preparing a variety of carbon compounds of metallic chlorides, which may, under appropriate conditions, possess a similar function. Slator found that in the chlorination of benzene in presence of stannic and ferric chloride the velocity is proportional to the concentration of the catalyst. Goldschmidt and Larsen have arrived at a similar result. From a study of the condensation of anisole with benzyl chloride they find the reaction to be unimolecular, and that the aluminium chloride acts as a catalyst increasing the velocity in proportion to its concentration. Steele concludes from similar observations 'that the action of aluminium and ferric chlorides in inducing the Friedel-Crafts reaction differs from many cases of true catalysis only in the accident that these reagents combine with certain substances produced during the reaction, and are thus removed from the system'. There are thus two processes at work—an activating process produced by the co-ordination of the catalyst with the original compound and a retarding action caused by the withdrawal of the catalyst in combination with the product. Both processes seem to follow from the researches of Olivier and Böseken on the interaction of p-bromobenzenesulphonyl chloride and benzene in that the aluminium chloride appears to be reactive only to the extent to which it is combined with the acid chloride, and part of the catalyst is removed in union with the product of the reaction. In spite of this fact the speed of the reaction is increased by an excess of free aluminium chloride, and cannot therefore be ascribed entirely to the co-ordinated compound of the catalyst.

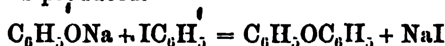
Ullmann's Method. Finely divided copper, although occasionally used in former years in place of silver, has recently been introduced by Ullmann and received extensive and important applications as a condensing agent.[1] The metal can be prepared by adding zinc dust to a solution of copper sulphate and carefully washing and drying the precipitate, but the commercial copper-bronze or finely divided metal, prepared mechanically, is better. The method is generally employed for removing halogens from the benzene nucleus. For example, iodobenzene is converted almost quantitatively at 230° into diphenyl; bromotoluene in the same way gives ditolyl. Bromobenzene and chloracetic ester when heated with finely divided copper to 180–200° are converted into phenylacetic ester. The reaction, in certain cases at least, is catalytic. Ortho-chlorobenzoic acid reacts with glycocoll to form phenylglycine-o-carboxylic acid; but the process is greatly accelerated by the addition of a minute quantity of copper powder. Similarly, a phenyl radical can be introduced into the amino group of amino acids and amides. By heating the potassium salt of anthranilic acid with bromobenzene and a little copper, phenylaminobenzoic acid is formed.



Potassium anthranilate. Phenylaminobenzoic acid.

[1] *Ber.*, 1901, **34**, 2174, 3802; 1903, **36**, 2382; 1904, **37**, 853; 1905, **38**, 729, 2120; 1906, **39**, 1691, 2211. *Annalen*, 1904, **332**, 38; 1906, **350**, 83.

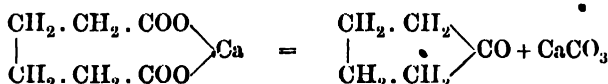
Phenyl iodide will also react with sodium phenate when a trace of copper is present, although in its absence not one per cent. of diphenyl ether is produced.



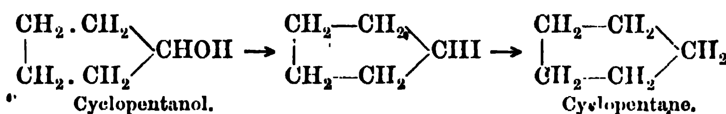
$$C_6H_5ONa + IC_6H_5 = C_6H_5OC_6H_5 + NaI$$

The above examples have been selected to illustrate the varied application of the method, which has proved to possess considerable technical importance.

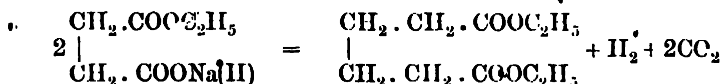
Removal of Carbon Dioxide. The well-known method of forming ketones by the distillation of calcium salts of organic acids has been utilised by J. Wislicenus[1] for the preparation of cyclic ketones by employing the calcium salts of dibasic acids. For this purpose, adipic,[2] pimelic, suberic,[3] azelaic and sebacic acids[4] have been used, giving cyclic ketones containing 5, 6, 7, 8 and 9 carbon atoms.



From these compounds the corresponding cycloparaffins may be obtained by reduction to the alcohol, conversion into the iodide, and reduction of the iodide with zinc and acetic acid.



The above method of distilling the calcium salts may be modified in certain cases with advantage by converting the dibasic acid into the anhydride and heating the latter.[5] The process of electrolysis may also effect condensation by removal of carbon dioxide and hydrogen. By way of illustration the following example may be taken, in which sodium ethyl succinate is converted into adipic ester.

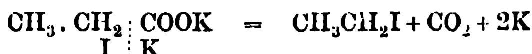


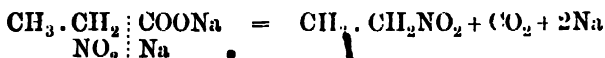
The application of the method in this way to the synthesis of the higher dibasic acids was first used by Crum-Brown and Walker,[6]

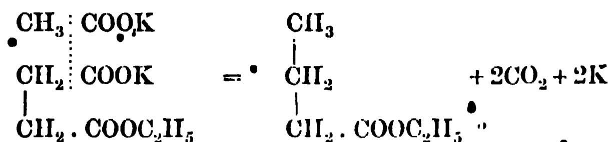
[1] *Annalen*, 1893, 275, 309.
[2] Montemartini, *Gazz. chim. ital.*, 1896, 26, 275.
[3] Blanc, *Compt. rend.*, 1907, 144, 1356.
[4] Derlon, *Ber.*, 1898, 31, 1962.
[5] Blanc, *Compt. rend.*, 1907, 144, 1356.
[6] *Annalen*, 1890, 261, 107; *Trans. Chem. Soc.*, 1896, 69, 1278.

and has since been studied by v. Miller,[1] and v. Miller and Hofer, who electrolysed mixtures of organic and inorganic salts.

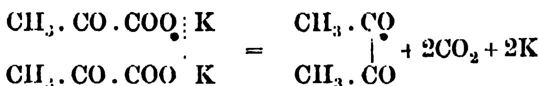
The following examples may serve to illustrate the reactions:



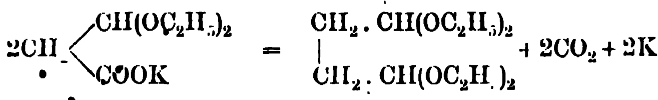




Hofer[2] afterwards electrolysed ketonic acids (pyruvic and levulinic) and obtained diketones.



Walker[3] found that by electrolysing sodium diethyl malonate two molecules link up to form the anhydride of tetraethylsuccinic acid, and Wohl and Schweitzer,[4] who submitted the sodium salt of acetal malonic aldehyde to the current, obtained the acetal of adipic aldehyde.



Group 2. Condensation by Addition.

Additive Reactions. Benzene under certain conditions forms additive compounds with unsaturated hydrocarbons, as in the union of styrene with benzene, which combine, giving diphenylethane,



or in that of benzene with cinnamic acid, which in presence of sulphuric acid yield diphenylpropionic acid,

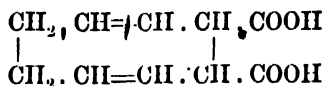


The production of cyclic structures have been observed in the case of acetylene, which when passed over finely divided iron gives small

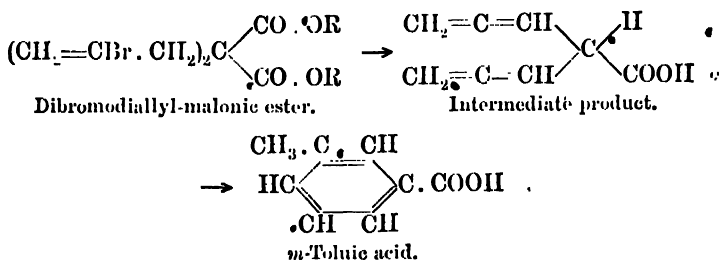
[1] *Zeit. f. Elektrochemie*, 1897, 4, 55; *Ber.*, 1895, 28, 2427.
[2] *Ber.*, 1900, 33, 650.
[3] *Trans. Chem. Soc.*, 1905, 87, 961.
[4] *Ber.*, 1906, 39, 890.

quantities of benzene;[1] of bromoacetylene, which exposed to light undergoes a similar change, yielding tribromobenzene; and of methyl- and dimethyl-acetylene, which in presence of strong sulphuric acid condense, forming respectively mesitylene and hexamethylbenzene.

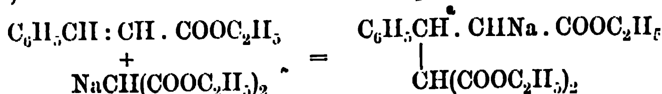
Döbner[2] has observed that vinylacrylic acid unites with itself, forming a ring compound of the formula



A very interesting case of ring formation by addition is recorded by Perkin,[3] in which dibromodiallyl-malonic ester on treatment with alcoholic potash is converted into *m*-toluic acid, a reaction which probably occurs in the following way:

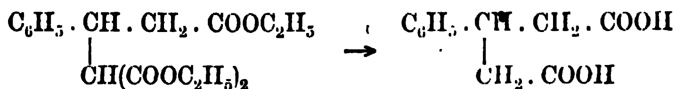


Michael's Reaction.[4] Michael has shown that the sodium compounds of acetoacetic ester and malonic ester are capable of forming additive compounds with unsaturated compounds of the general formula: R.CH:CHX or R.C:C.X, in which R is a positive or negative organic radical, and X a strongly negative radical such as carbonyl, cyanogen, &c. The sodium attaches itself to the carbon atom linked to the negative group and the negative radical to the positive carbon group. The first example studied by Michael was the condensation of sodium malonic ester (prepared by the action of metallic sodium or dry sodium ethoxide on the ester dissolved in ether) on cinnamic ester. The union takes place in the following way:



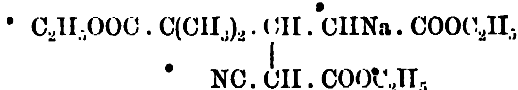
[1] Moissan and Moureu, *Compt. rend.*, 1896, 122, 1240; see also *Compt. rend.*, 1900, 130, 1319, and *Chem. Centralbl.*, 1902, I, 77.
[2] *Ber.*, 1902, 35, 2129.
[3] *Trans. Chem. Soc.*, 1907, 91, 816, 840, 848.
[4] Michael, *J. prakt. Chem.*, 35, 351; 43, 395; 45, 55; 49, 20; Auwers, *Ber.*, 1891, 24, 317, 2887; 1893, 26, 364; 1895, 28, 263; Ruhemann and Cunnington, *Trans. Chem. Soc.*, 1898, 73, 1006.

Acids liberate the tribasic ester which, by hydrolysis, can be converted into the dibasic β-phenylglutaric acid,

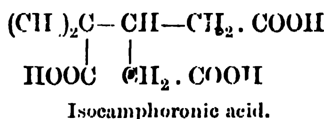


Fumaric, maleic, aconitic, crotonic, citraconic, and itaconic esters, acetylene dicarboxylic and phenylpropiolic esters and benzylidene acetone, &c., behave in the same way, though there is a considerable difference in the rate of formation.[1]

The sodium compound of cyanacetic ester resembles malonic ester[2] and has been utilized by Perkin[3] for the synthesis of isocamphoronic acid. Dimethylglutaconic ester, when digested with an alcoholic solution of sodium cyanacetic ester, yields:

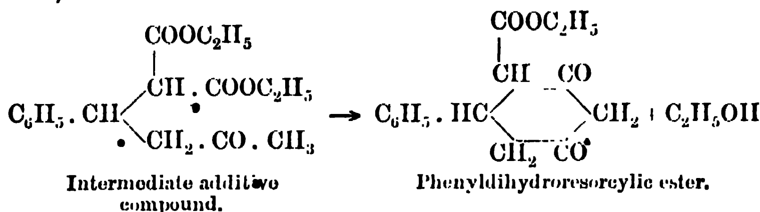


If the resulting ester is then hydrolysed, isocamphoronic acid is obtained, which consequently has the formula:



Isocamphoronic acid.

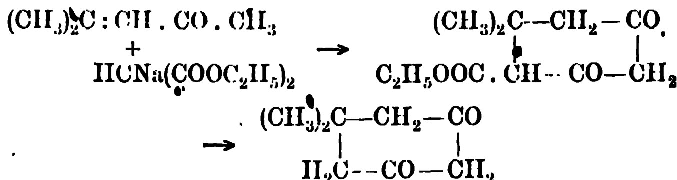
The same condensation process has also been applied to the synthesis of cyclic compounds by Vorländer.[4] Benzylidene acetone combines with sodium malonic ester, forming phenyldihydroresorcylic ester,[5]



Intermediate additive compound. Phenyldihydroresorcylic ester.

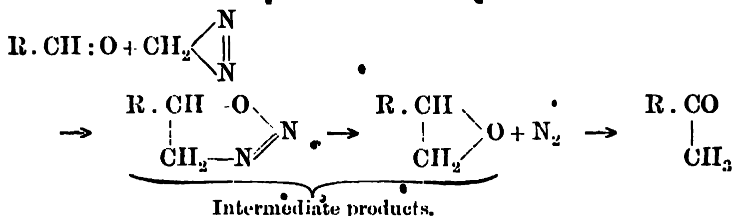
In the same way mesityl oxide may be converted into dimethyldiketocyclohexane,

[1] Auwers, *Ber.*, 1895, 28, 1131; *Annalen*, 1896, 292, 147.
[2] Müller, *Compt. rend.*, 1892, 114, 1204; Noyes, *Ber.*, 1899, 32, 2289.
[3] *Proc. Chem. Soc.*, 1900, 214.
[4] *Ber.*, 1894, 27, 2053; *Annalen* 1896, 294, 253.
[5] In both these reactions the compound in the second stage undergoes the acetoacetic ester condensation (see p. 220).



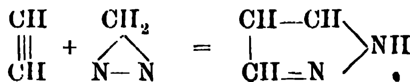
and Knoevenagel has prepared isoacetophorone in the same fashion, using sodium acetoacetic ester in place of sodium malonic ester. Knoevenagel [1] also found that diethylamine could replace sodium or sodium ethoxide in effecting condensations of this character.

Buchner-Curtius Reaction. This reaction yields in the first instance pyrazole derivatives, which, by loss of nitrogen, may be converted into true condensation products. A simple illustration of the reaction is furnished by the union of an aldehyde with diazomethane, forming a ketone by elimination of nitrogen, [2]



A more interesting application of the method is the preparation of those pyrazole compounds which yield cyclopropane derivatives by loss of nitrogen.

It is well known that acetylene combines directly with diazomethane, giving pyrazole, [3]



Acetylene dicarboxylic ester combines in a similar way with diazomethane, the resulting product being pyrazole dicarboxylic ester. Now, if in place of acetylene or its dicarboxylic ester, esters of the olefine acids such as fumaric, maleic, and aconitic esters be substituted, pyrazole compounds are formed as before, but readily lose nitrogen on heating, and the ring closes up and gives a cyclic compound.

Fumaric ester and diazomethane react, giving cyclopropane dicarboxylic ester, as follows:

[1] *Ber.*, 1904, 37, 4461. [2] Schlotterbeck, *Ber.*, 1907, 40, 479. [3] v. Pechmann, *Ber.*, 1898, 31, 2950.

$$\begin{matrix} CH_2 & CH.COOC_2H_5 \\ / \backslash & + \| \\ N{=}N & CH.COOC_2H_5 \end{matrix} \rightarrow \begin{matrix} CH_2-CH.COOC_2H_5 \\ | \quad\quad | \\ N \quad CH.COOC_2H_5 \\ \backslash\backslash\ / \\ N \end{matrix}$$

$$\rightarrow \begin{matrix} CH_2-CH.COOC_2H_5 \\ \diagdown\ | \\ CH.COOC_2H_5 \end{matrix} + N_2$$

If, in place of diazomethane, diazoacetic ester is used, a cyclopropane tricarboxylic ester is formed.[1]

Addition of Hydrogen Cyanide. The addition of hydrogen cyanide to aldehydes and ketones giving cyanhydrins affords an extremely useful method for the preparation of hydroxy acids containing an additional carbon atom in the chain. The addition of this reagent is not restricted to the CO group; for it is found that in unsaturated ketones and acids containing the grouping C:C.CO hydrogen cyanide will attach itself by preference to the double bond, thus forming ketonic cyanides and ketonic acids.[2] Benzalmalonic ester combines as follows:

$$C_6H_5CH:C\begin{matrix} \diagup COOC_2H_5 \\ \diagdown COOC_2H_5 \end{matrix} + HCN = C_6H_5\underset{\displaystyle CN}{\underset{|}{CH}}.CH\begin{matrix} \diagup COOC_2H_5 \\ \diagdown COOC_2H_5 \end{matrix}$$

Organo-metallic Compounds. The extraordinary development which organic synthesis owes to the use of organo-metallic compounds has its origin in Frankland's discovery of the zinc alkyl compounds. The preparation of these compounds need not be described. They are extremely unstable liquids which are characterised by their strong affinity for either free or combined oxygen and for the halogens. It is on these properties that their manifold transformations depend. Paraffins may be derived from them either by the direct action of water,[3] of alkyl iodides, or of dihalogen compounds.[4] The following reactions illustrate each of the methods:

$$Zn(CH_3)_2 + 2H_2O = 2CH_4 + Zn(OH)_2$$
$$Zn(CH_3)_2 + 2(CH_3)_3CI = 2(CH_3)_4C + ZnI_2$$
$$Zn(CH_3)_2 + CH_3.CCl_2.CH_3 = C(CH_3)_4 + ZnCl_2$$

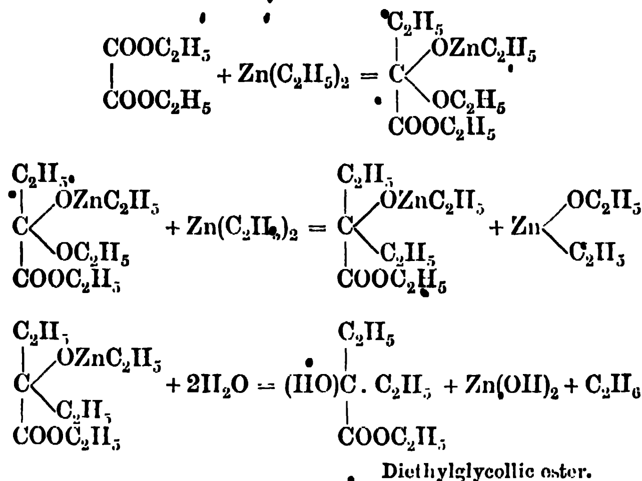
1 Buchner and Curtius, *Ber.*, 1885, 18, 237.

2 Lapworth, *Trans. Chem. Soc.*, 1903, 83, 995; 1904, 85, 1206, 1214; 1906, 89, 945; Brest and Kallen, *Annalen*, 1896, 293, 338.

3 Frankland, *Annalen*, 1849, 71, 203; 1850, 74, 41.

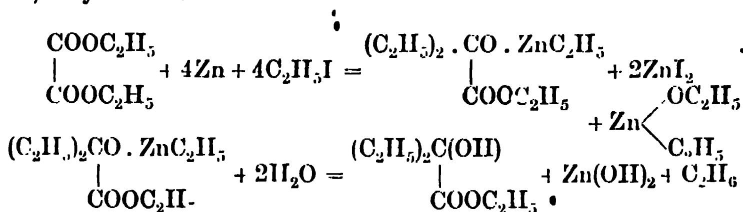
4 Friedel and Ladenburg, *Annalen*, 1867, 142, 316; Lwow, *Zeits.*, 1871, 257.

Zinc Alkyl Condensations (Frankland's Method). The discovery by Frankland and Duppa[1] of the formation of a hydroxy acid from zinc ethyl and oxalic ester prepared the way for new and unlooked-for synthetic uses of the zinc alkyl compounds. If to one molecule of ester two molecules of zinc alkyl are added and the product decomposed by water, diethylglycollic ester is obtained. The following equations represent the course of the reaction:



Diethylglycollic ester.

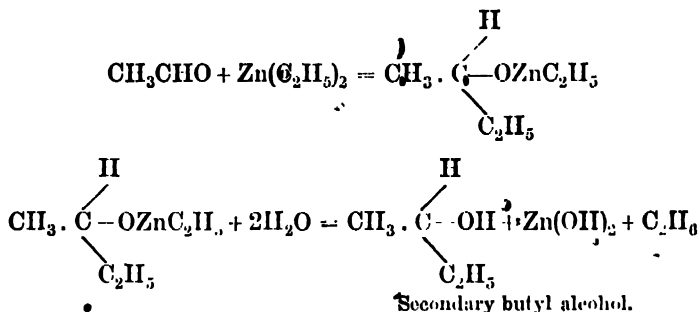
The same product was also prepared by heating a mixture of oxalic ester, alkyl iodide, and zinc.[2]



This was followed by the researches of Wagner,[3] on the action of zinc alkyl on aldehydes, which led to the synthesis of secondary alcohols; of Saytzeff,[4] who applied a similar reaction to the ketones and obtained tertiary alcohols; of Butlerow,[5] who prepared alcohols from the acid chlorides; of Freund,[6] who obtained ketones from the

[1] *Annalen*, 1863, 126, 109.
[2] Frankland and Duppa, *Annalen*, 1863, 126, 109; 1868, 135, 26.
[3] *Annalen*, 1876, 181, 261.
[4] *Annalen*, 1877, 185, 151.
[5] *Annalen*, 1867, 144, 1.
[6] *Annalen*, 1861, 118, 3.

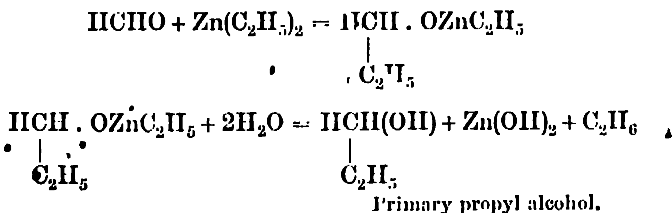
acid chlorides; of Wagner, Saytzeff, and Kannonikoff,[1] who converted aliphatic esters into secondary and tertiary alcohols. The following examples illustrate the different types of reactions referred to. Aldehydes and zinc alkyls form secondary alcohols. Acetaldehyde and zinc ethyl yield secondary butyl alcohol.



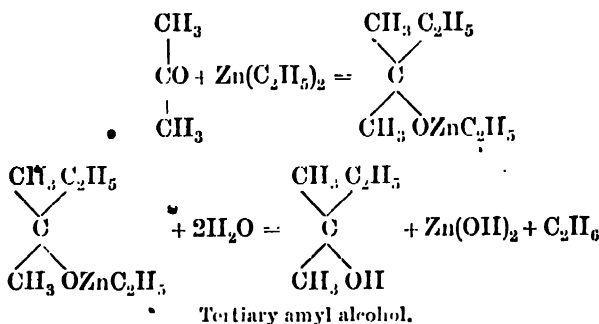
Secondary butyl alcohol.

Formaldehyde gives primary alcohols by a similar series of changes, whereas ketones yield tertiary alcohols.

Formaldehyde and zinc ethyl yield primary propyl alcohol, whilst acetone and zinc ethyl give tertiary amyl alcohol.



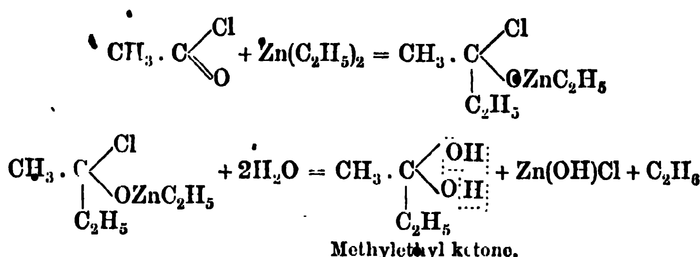
Primary propyl alcohol.



Tertiary amyl alcohol.

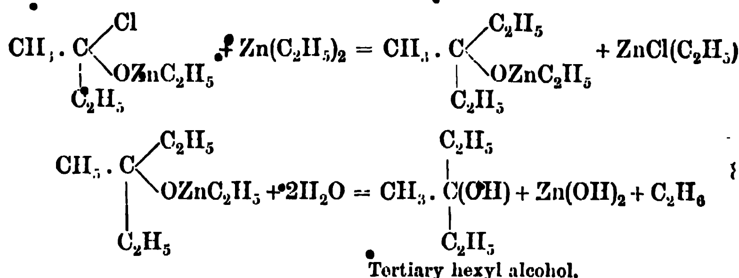
Acid chlorides react with one and two molecules of zinc alkyl. Acetyl chloride and zinc ethyl form methylethyl ketone.

[1] *Annalen*, 1875, 175, 351; 1877, 185, 129, 148, 169.



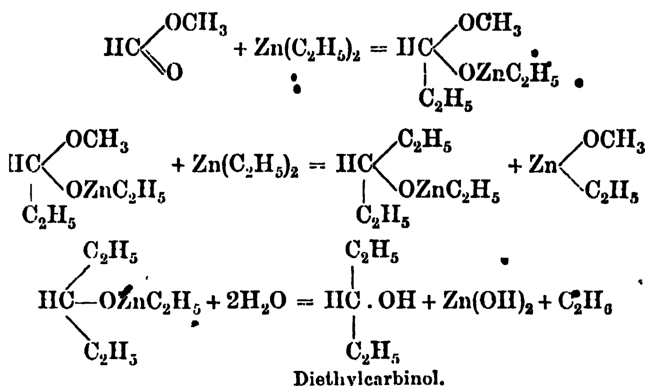
Methylethyl ketone.

If the intermediate product is allowed to react with a second molecule of zinc alkyl, a tertiary alcohol results.



Tertiary hexyl alcohol.

With the esters a similar process occurs. Methyl formate and two molecules of zinc ethyl yield a secondary butyl alcohol. The reaction occurs in two steps.



Diethylcarbinol.

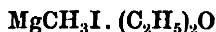
Other fatty esters like acetic ester will naturally yield tertiary alcohols by this process.

Magnesium Alkyl Condensations (Grignard's Reaction). The use of magnesium in place of zinc for introducing radicals into organic compounds in the manner employed by Frankland and Duppa

was first suggested in 1899 by Barbier,[1] who converted methylheptenone into a tertiary alcohol by the action of methyl iodide in presence of magnesium. In the following year the study of the preparation and synthetic uses of magnesium alkyl compounds was taken up by Grignard, who published an account of his results in the *Comptes rendus*.[2] Since then the reaction has been applied by himself and his collaborators, as well as by a host of other workers, in so many directions that it will be impossible to do more than indicate the nature of the main applications of this interesting and useful synthetic process. For a more complete account the references given in the footnote may be consulted.[3]

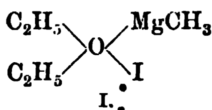
Although the behaviour of the magnesium alkyl compounds will be seen to resemble in many respects that of the zinc alkyls, their greater reactivity, owing no doubt to the more electropositive character of the metal, as well as the convenience of their preparation, offer great advantages over the use of the zinc compounds. Moreover, aromatic halogen compounds, such as bromo- and iodobenzene and toluene, may be used in addition to the alkyl halides.

The method of preparation consists in adding to one atomic proportion of clean metallic magnesium wire, ribbon, or filings, suspended in perfectly dry ether, a molecular equivalent of the alkyl iodide or bromide (or phenyl or tolyl bromide), also dissolved in ether. The magnesium dissolves with evolution of heat, and a solution is usually obtained which contains the magnesium alkyl or aryl bromide or iodide. If methyl iodide is used, and, after the action is complete, the excess of ether is evaporated and the product heated to 100–120° in a vacuum to remove the last traces of solvent, the composition of the residue is found to correspond to a substance of the formulae:

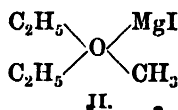


$$MgCH_3I \, . \, (C_2H_5)_2O$$

The ether was regarded by Grignard as ether of crystallization, but Baeyer and Villiger regarded it as part of a compound containing quadrivalent oxygen (I). Grignard afterwards adopted the view, but distributed the magnesium alkyl halide differently (II)



I.



II.

There are reasons for supposing that the ether plays an essential

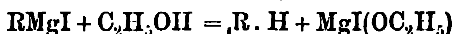
[1] *Compt. rend.*, 1899, 128, 110. [2] *Compt. rend.*, 1900, 130, 1322.
[3] J. Schmidt, Ahrens' *Vorträge*, 1905, 10, 68; A. McKenzie, *Brit. Ass. Reports* 1907, p. 273; *Amer. Chem. Journ.*, 1905, 33, 318.

part in the synthetic process to which the magnesium compound is applied, but discussion of the mechanism of the reaction is reserved until some of its more important applications have been considered.

Hydrocarbons. The magnesium alkyl or aryl iodide is decomposed by water or alcohol, or indeed by any compound which contains a hydroxyl group, giving a hydrocarbon.

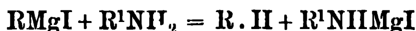


$$RMgI + H_2O = R.H + MgI(OH)$$



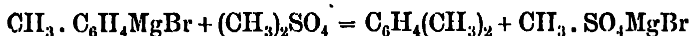
$$RMgI + C_2H_5OH = R.H + MgI(OC_2H_5)$$

The method has been applied to the estimation of hydroxyl groups in organic compounds.[1] Ammonia and primary amines react in the same way by giving up hydrogen to the radical and entering into union with the magnesium halide.



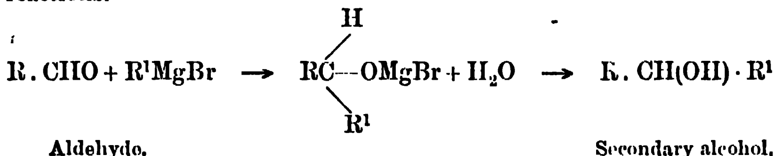
$$RMgI + R^1NH_2 = R.H + R^1NHMgI$$

A methyl group may be introduced into an aromatic hydrocarbon by employing the aryl magnesium bromide in conjunction with methyl sulphate (Werner and Zilkens).



$$CH_3.C_6H_4MgBr + (CH_3)_2SO_4 = C_6H_4(CH_3)_2 + CH_3.SO_4MgBr$$

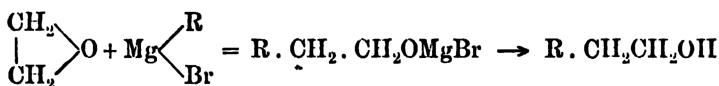
Alcohols may be obtained from aldehydes, ketones, acid chlorides, esters, &c., by methods which offer a close analogy to the zinc alkyl reactions.



$$R.CHO + R^1MgBr \rightarrow RC(H)(R^1)\text{—}OMgBr + H_2O \rightarrow R.CH(OH).R^1$$

Aldehyde. Secondary alcohol.

Primary alcohols can be obtained from formaldehyde, or more conveniently from its polymeric form, trioxymethylene. They have also been prepared from ethylene oxide and ethylene chlorhydrin (Blaise). In the first case the action takes place by cleavage of the ring:



$$\begin{matrix}CH_2\\|\\CH_2\end{matrix}\!>\!O + Mg\!<\!\begin{matrix}R\\Br\end{matrix} = R.CH_2.CH_2OMgBr \rightarrow R.CH_2CH_2OH$$

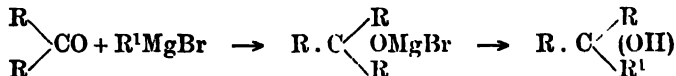
In the second case it occurs in two phases, the hydroxyl group being first attacked and then the halogen, on addition of a second molecule of reagent.

[1] Hibbert and Sudborough, *Trans. Chem. Soc.*, 1904, 85, 933; Zerewitinoff, *Ber.*, 1907, 40, 2023.

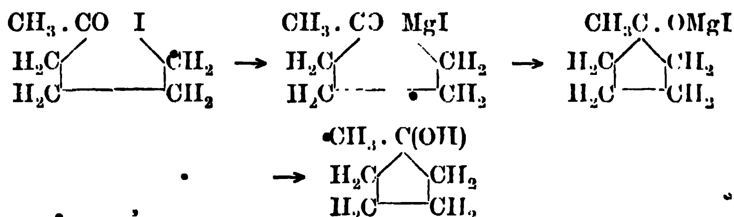




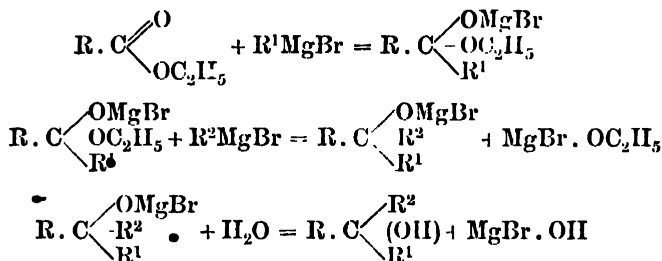
Tertiary alcohols are readily prepared from ketones, esters, and acid chlorides.



The process may be applied to cyclic ketones, ketonic acids, diketones, and quinones. In the last two cases the reaction may be regulated so that either one or both ketone groups are involved. It is an interesting fact that a tautomeric ketonic ester, such as acetoacetic ester, reacts in the enol form, that is, forms an additive compound with the reagent, which is decomposed by water and the ester regenerated. If alkyl groups are introduced, the ester then behaves as a ketone. This reaction has been applied to the formation of cyclic compounds by Zelinsky and Moser[1] in the following ingenious way, from *w*-acetobutyl iodide.



Esters react as follows:



In the case of dibasic esters, both ester groups will react, forming glycols. If formic ester is used, a secondary alcohol results.

Acid chlorides react, as in the case of the zinc alkyl compounds, in two phases, giving ketones in the first and tertiary alcohols in the second. Carbonyl chloride behaves in a similar fashion:

[1] *Ber.*, 1902, 35, 2684.



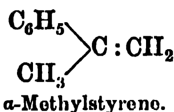
$$COCl_2 + 3RMgBr = CR_3OMgBr + MgCl_2 + MgBr_2$$



$$CR_3OMgBr + H_2O = R_3C(OH) + Mg(OH)Br$$

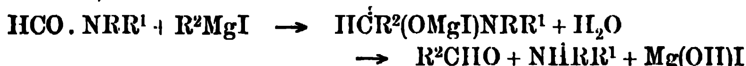
Anhydrides and lactones also give tertiary alcohols.

It frequently happens that, in the reactions with aldehydes and ketones, an unsaturated hydrocarbon appears in place of the alcohol. This must be ascribed to a secondary process (whereby water is eliminated), which it is often possible to promote or prevent by modifying the conditions. Acetophenone, for example, may be made to yield the unsaturated hydrocarbon in place of the alcohol by raising the temperature at the end of the process.



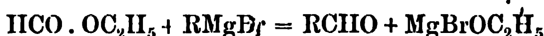
α-Methylstyrene.

Aldehydes. Quite a number of methods have been elaborated for producing aldehydes, of which the following are the most important. By the use of dimethylformamide the following changes occur (Bouveault):



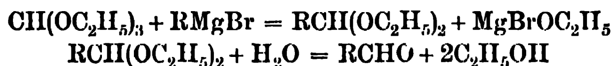
$$HCO.NRR^1 + R^2MgI \longrightarrow HCR^2(OMgI)NRR^1 + H_2O \longrightarrow R^2CHO + NHRR^1 + Mg(OH)I$$

Under ordinary conditions the effect of the Grignard reagent on formic ester is to give a secondary alcohol, but Gattermann found that by using three molecules of ester and keeping the temperature low, the aldehyde is formed (Gattermann).



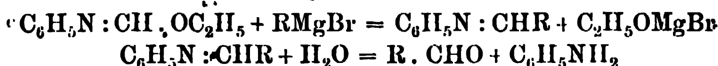
$$HCO.OC_2H_5 + RMgBr = RCHO + MgBrOC_2H_5$$

Orthoformic ester may also be used (Boudroux).



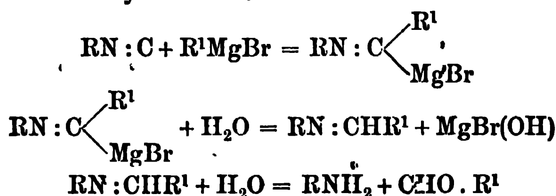
$$CH(OC_2H_5)_3 + RMgBr = RCH(OC_2H_5)_2 + MgBrOC_2H_5$$
$$RCH(OC_2H_5)_2 + H_2O = RCHO + 2C_2H_5OH$$

Gattermann introduced ethoxymethylene aniline in place of ethyl formate, the reaction taking place as follows:



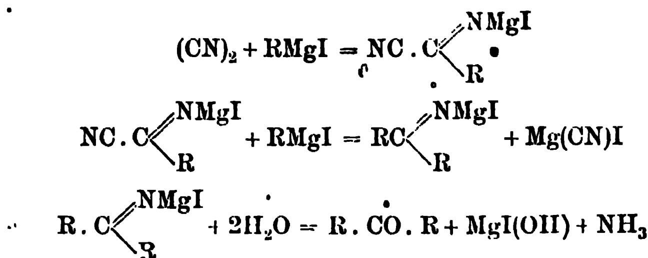
$$C_6H_5N:CH.OC_2H_5 + RMgBr = C_6H_5N:CHR + C_2H_5OMgBr$$
$$C_6H_5N:CHR + H_2O = R.CHO + C_6H_5NH_2$$

Another method which also yields aldehydes is that of Sachs and Loevy in which isocyanides are used.

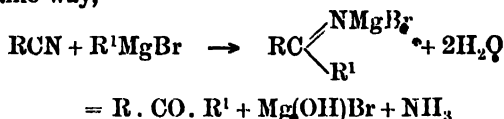


$$RN:C + R^1MgBr = RN:C\begin{matrix}R^1\\MgBr\end{matrix}$$
$$RN:C\begin{matrix}R^1\\MgBr\end{matrix} + H_2O = RN:CHR^1 + MgBr(OH)$$
$$RN:CHR^1 + H_2O = RNH_2 + CHO.R^1$$

Ketones can be prepared from cyanogen, cyanides, and amides.

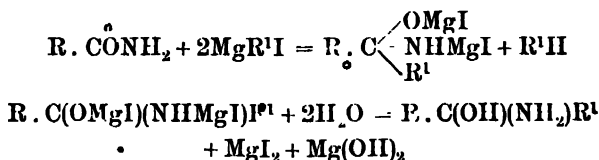


In the same way,



Ketonic esters may be obtained by the same process from cyanogen esters. Cyanacetic ester, for example, with magnesium methyl iodide yields acetoacetic ester (Blaise).

The action upon amides is represented as follows:

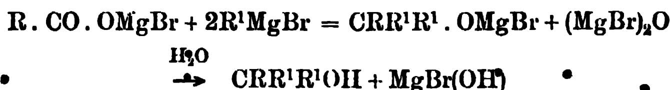


The last product loses ammonia and gives the ketone.

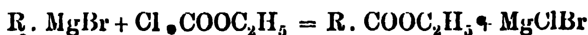
Acids and Esters. Acids are obtained by passing carbon dioxide into the ethereal solution of the magnesium alkyl compound and decomposing the product with water or sulphuric acid, or, if the sodium salt is required, with sodium hydroxide solution (Grignard).



If the intermediate compound is further acted upon by two molecules of magnesium alkyl halide, and the product decomposed with water, a tertiary alcohol is formed.

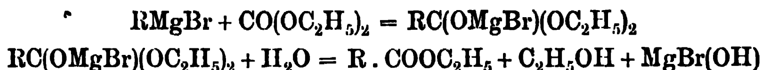


By using chloroformic ester with the Grignard reagent, esters are obtained (Houben).



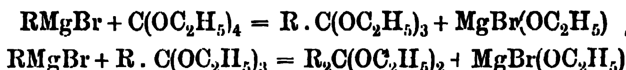
The reaction may proceed to a second phase, yielding a tertiary alcohol, as already explained (p. 211).

Carbonic esters may also be used in the preparation of esters (Tschitschibabin).



$$RMgBr + CO(OC_2H_5)_2 = RC(OMgBr)(OC_2H_5)_2$$
$$RC(OMgBr)(OC_2H_5)_2 + H_2O = R.COOC_2H_5 + C_2H_5OH + MgBr(OH)$$

Ortho-carbonic ester reacts in a similar manner.



$$RMgBr + C(OC_2H_5)_4 = R.C(OC_2H_5)_3 + MgBr(OC_2H_5)$$
$$RMgBr + R.C(OC_2H_5)_3 = R_2C(OC_2H_5)_2 + MgBr(OC_2H_5)$$

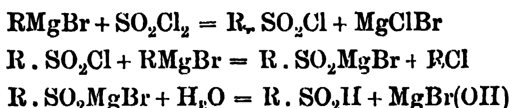
In this case an acetal is formed.

Sulphur Acids. Sulphur dioxide reacts like carbon dioxide and forms sulphinic acids (Rosenheim and Singer).



$$RMgBr + SO_2 \longrightarrow R.SO_2MgBr \xrightarrow{H_2O} R.SO_2H + MgBr(OH)$$

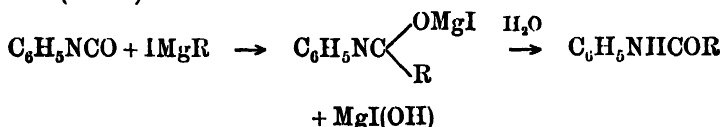
The same product is obtained from sulphuryl chloride (Oddo).



$$RMgBr + SO_2Cl_2 = R.SO_2Cl + MgClBr$$
$$R.SO_2Cl + RMgBr = R.SO_2MgBr + RCl$$
$$R.SO_2MgBr + H_2O = R.SO_2H + MgBr(OH)$$

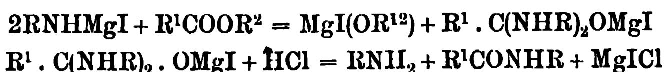
Carbithionic acids are formed by the action of carbon bisulphide on the reagent in the same way as the carboxylic acids by the use of carbon dioxide (Houben).

Amides of the aromatic series may be obtained from aryl carbimides (Blaise).



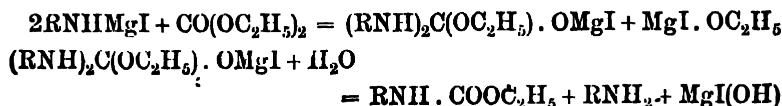
$$C_6H_5NCO + IMgR \longrightarrow C_6H_5NC{<}^{OMgI}_{R} \xrightarrow{H_2O} C_6H_5NHCOR + MgI(OH)$$

Similar products are obtained by forming the magnesium compound of a primary aromatic amine, RNHMgI, and acting upon it with the ester of a monobasic acid (Bodroux).



$$2RNHMgI + R^1COOR^2 = MgI(OR^{12}) + R^1.C(NHR)_2OMgI$$
$$R^1.C(NHR)_2.OMgI + HCl = RNH_2 + R^1CONHR + MgICl$$

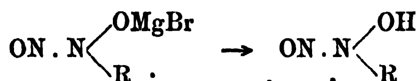
If, in place of a monobasic ester, ethyl carbonate is substituted, a urethane is formed (Bodroux).



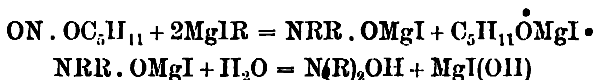
$$2RNHMgI + CO(OC_2H_5)_2 = (RNH)_2C(OC_2H_5).OMgI + MgI.OC_2H_5$$
$$(RNH)_2C(OC_2H_5).OMgI + H_2O = RNH.COOC_2H_5 + RNH_2 + MgI(OH)$$

Thioanilides are obtained by substituting mustard oils for the carbimides in the above reaction (Sachs and Loevy).

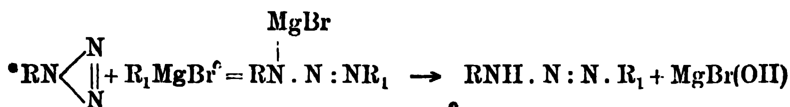
Hydroxylamine Derivatives. Both nitric oxide and nitrogen peroxide react with the Grignard reagent, the former giving nitroso hydroxylamines and the latter dialkyl hydroxylamines (Wieland).



The mechanism of the second reaction has not been explained, but is no doubt due to partial reduction of the peroxide by the reagent. Hydroxylamine derivatives may also be obtained from amyl nitrite as follows:



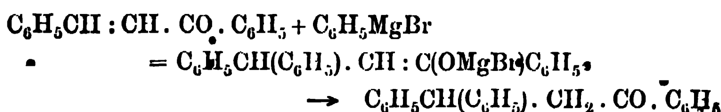
Diazoamino-compounds. Aliphatic as well as aromatic diazoamino-compounds can be prepared from alkyl and aryl azides.[1]



Additive Compounds. Kohler[2] has made a careful study of the action of the Grignard reagent on the unsaturated aldehydes and ketones containing the group C : C . CR : O. Several reactions are possible. Addition may occur at the double bond or with the ketone or aldehyde group, or again, following Thiele's rule (p. 133), in the 1 . 4 position. All these effects have been observed and are found to depend upon the nature of the attached radicals and may be summarized as follows:

1. In aldehydes and ketones in which R is hydrogen or an alkyl group, a normal reaction with the CO group takes place, with the formation of a tertiary alcohol.

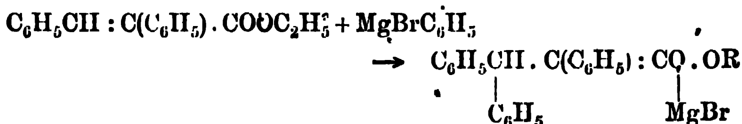
2. If the attached radical is aromatic, addition occurs in position 1 . 4, and a ketone is formed, as in the case of cinnamylphenyl ketone.

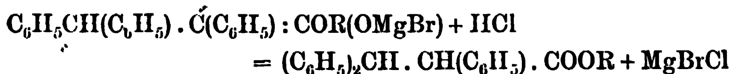


[1] Dimroth, *Ber.* 1906, 39, 3905.
[2] *Amer. Chem. Journ.*, 1905, 33, 153, 333 ; 34, 132.

3. If the attached radical is an alkyl-oxy group, that is, if the compound is an unsaturated ester, addition either takes place as in (2) or the alkyl-oxy group is replaced by the radical of the reagent. The former occurs with an aryl magnesium halide, and the latter with an alkyl compound.

For example, phenylcinnamic ester reacts as follows with phenyl magnesium bromide:

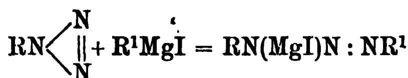


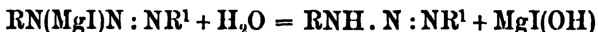


Additive compounds are also formed with unsaturated nitrogen compounds such as benzylidene aniline,



which yields the secondary amine on decomposition with water (Busch). Oximes behave similarly, the radical attaching itself to the unsaturated carbon and the magnesium halide to the nitrogen. Triazo-compounds also react by cleavage of the nitrogen ring, followed by the formation of diazoamino-compounds (Dimroth).

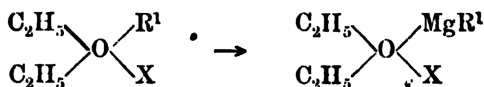




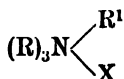
The reaction may be applied indifferently to the preparation of both aliphatic and aromatic compounds.

This does not exhaust the many changes which may be rung on the reaction, but the above examples will serve to illustrate the general character of the process. It will be seen that, apart from the simplicity and convenience of the method, the magnesium compounds are much more reactive than the zinc alkyls, and their combination may be effected with nitrogen much in the same way as with oxygen, thereby increasing the range of their application. It should be observed that the metal always attaches itself to the more electronegative element (O and N), either by adding itself to the latter if unsaturated, or by replacing the hydrogen when combined as hydroxyl or amino groups.

It has been suggested by Tschelinzeff[1] that the ether which appears to form a compound with the magnesium alkyl halide acts catalytically at low temperatures, for although interaction between the magnesium and alkyl halide takes place in benzene or xylene, it is necessary to boil the liquid, whereas the presence of a little ethyl or amyl ether or anisole (methylphenyl ether) causes combination at the ordinary temperature. He considers the effect of the ether is to dissociate the alkyl halide by forming the oxonium compound, thus assisting union with the metal:

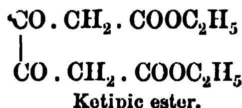


Tertiary amines such as dimethylaniline may replace ether as the catalyst, and their reaction is explained in a similar way by the disruption of the alkyl halide R^1X from the quinquevalent compound.



A further examination of the ether compounds of the alkyl magnesium halide has shown that the latter unites with two molecules of ether, corresponding thus to Zelinsky's compound with magnesium iodide $MgI_2 . 2(C_2H_5)_2O$. The evidence for this was given by Tschelinzeff, who showed that on adding ether to a benzene solution of magnesium alkyl iodide, equal quantities of heat are evolved for each of the first two molecular proportions of ether added.

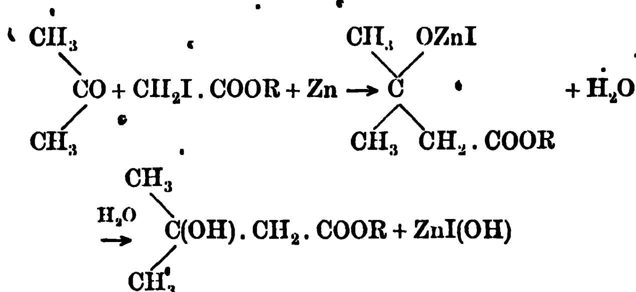
Reformatsky's Reaction. A reaction which may be regarded as a modification of Frankland's and Grignard's was first suggested by Fittig and Daimler.[2] They attempted to combine chloracetic ester with oxalic ester in presence of zinc, in the expectation of obtaining a product similar to that of Frankland, in which the acetic ester group would play the part of an alkyl radical. The reaction, however, gave instead ketipic (keto-adipic) ester.



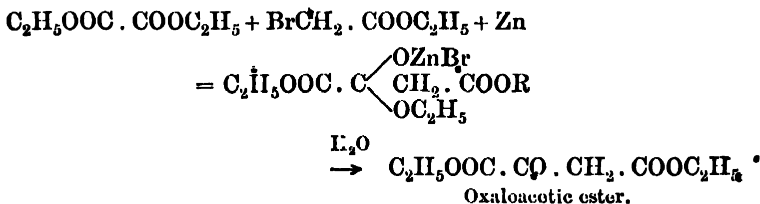
Ketipic ester.

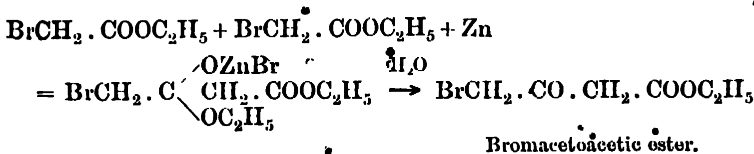
Reformatsky[3] was afterwards more successful, and obtained a β-hydroxy-isovaleric ester from acetone, iodoacetic ester and zinc.

[1] *Ber.*, 1904, 37, 2084; see also v. Braun, *Ber.*, 1919, 52, 1725.
[2] *Ber.*, 1887, 20, 202.
[3] *Ber.*, 1887, 20, 1210; 1895, 28, 2163, 2838.



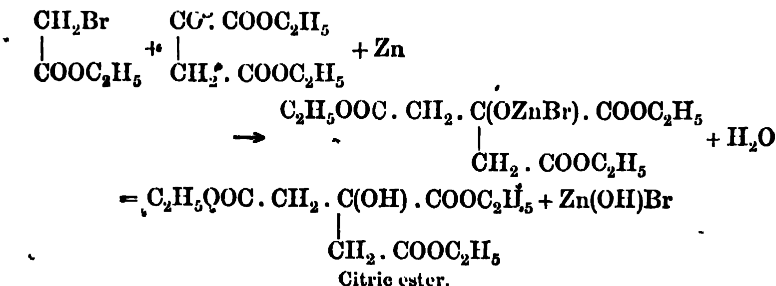
Lapworth has shown that the ester group behaves in the manner of a ketone group, and has succeeded in condensing oxalic ester with bromacetic ester, and also two molecules of bromacetic ester with zinc or magnesium, with the object of throwing light on the aceto-acetic ester synthesis, to be presently discussed.





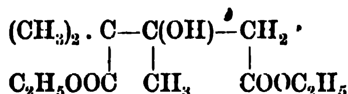
The reaction has since been used for the synthesis of citric acid by Lawrence,[1] *dl*-camphoronic acid by Perkin[2] and by others for similar condensations (see Part III, p. 235).

In the first case, union is effected between bromacetic ester and oxaloacetic ester, and proceeds as follows:

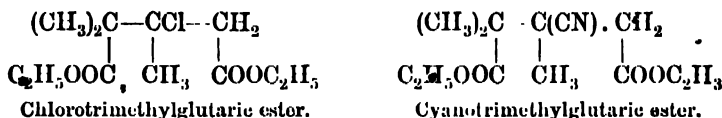


[1] *Trans. Chem. Soc.*, 1897, 71, 457. [2] *Trans. Chem. Soc.*, 1897, 71, 1173.

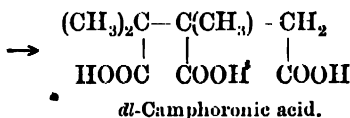
In the second synthesis, α-bromoisobutyric ester and acetoacetic ester or bromacetic ester and dimethylacetoacetic ester in presence of zinc were first combined, giving hydroxytrimethylglutaric ester.



The compound was then acted on with phosphorus pentachloride and converted into chlorotrimethylglutaric ester. On boiling with alcoholic potassium cyanide, cyanotrimethylglutaric ester is formed, and, finally, on hydrolysing with hydrochloric acid, *dl*-camphoronic acid.



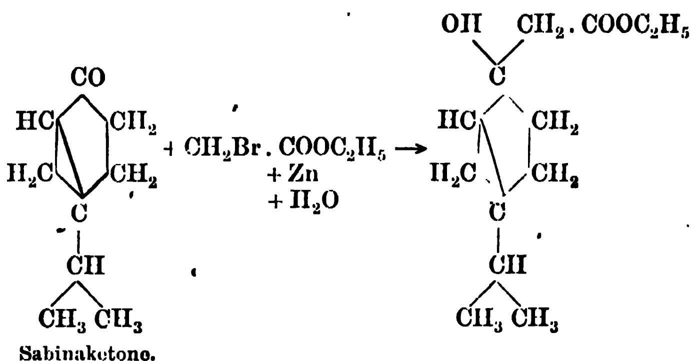
Chlorotrimethylglutaric ester. Cyanotrimethylglutaric ester.



dl-Camphoronic acid.

Magnesium has been used in place of zinc in the above reaction.[1]

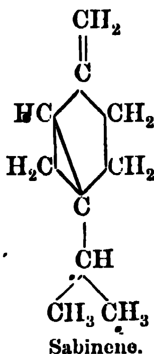
Wallach[2] has utilised the reaction for introducing unsaturated side-chains into cyclic ketones. Sabinaketone can be converted into sabinene in the following way:



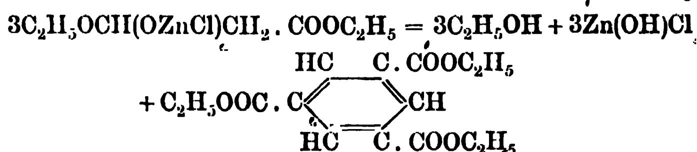
Sabinaketone.

The latter, when heated with acetic anhydride, loses carbon dioxide and alcohol and gives:

[1] Zelinsky and Gutt, *Ber.*, 1902, 35, 2140.
[2] *Annalen*, 1908, 360, 26; 1909, 365, 255.

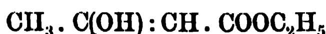

Sabinene.

An example of ring formation is recorded by Reformatsky,[1] who obtained trimesic ester by condensing formic ester with chloracetic ester and zinc.



The Acetoacetic Ester Condensation (*Union of*—$COOC_2H_5$ + $CH_2 . COOC_2H_5$). The discovery of acetoacetic ester carries us back to the year 1863, when Geuther,[2] who held the view that acetic acid contains two hydrogen atoms replaceable by metals, sought to replace the second hydrogen atom in ethyl acetate (since it could not be effected with sodium acetate) by means of metallic sodium.

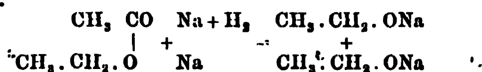
He observed the evolution of hydrogen,[3] the formation of sodium ethoxide, and the production of a crystalline sodium compound of the formula $C_6H_9NaO_3$. From the sodium compound, by the addition of an acid, a liquid was isolated which, though neutral to litmus, formed salts with metallic bases. He found, moreover, that the sodium of the sodium compound reacts with alkyl iodides and forms a series of alkyl ethers. These facts led Geuther to name the new compound *ethyldiacetic acid*, and to represent it by the formula:



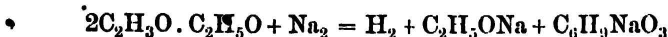
$$CH_3 . C(OH) : CH . COOC_2H_5$$

[1] *J. russ. phys. chem. Ges.*, 1898, 30, 280. [2] *Jahresb.*, 1863, 323.

[3] It was subsequently found that when ethyl acetate is pure, little, if any, hydrogen is evolved, but according to Oppenheim and Precht (*Ber.*, 1876, 9, 320) it is used in conjunction with sodium to convert some of the acetic ester into sodium ethoxide.



The formation of the sodium salt was represented by the equation :



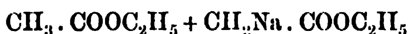
$$2C_2H_3O.C_2H_5O + Na_2 = H_2 + C_2H_5ONa + C_6H_9NaO_3$$

Whilst this research was in progress Frankland and Duppa were studying the action of alkyl iodides on oxalic ester in presence of zinc. In extending their investigations to ethyl acetate, the zinc was replaced by the more energetic metal, sodium, and, during the solution of the metal in the ester, the evolution of hydrogen was observed. Without isolating the product they proceeded to heat up the solid mass with ethyl iodide. In this way various products were obtained and separated by fractional distillation. Among them four compounds boiling between 120° and 265° were isolated and characterized as follows : (1) *butyric ester*, (2) *diethylacetic ester*, (3) a compound identical with the ethyl ester of Geuther's ethyldiacetic acid, which, since it decomposed with alkalis into ethyl acetone, alcohol, and carbon dioxide, was termed *ethacetone carbonate of ethyl*, and (4) a final fraction which decomposed in the same manner into diethyl acetone, alcohol, and carbon dioxide, and received the name of *diethacetone carbonate of ethyl*. Frankland and Duppa explained the formation of the first two compounds by supposing that ethyl acetate is converted by sodium into a mono- and di-sodium ethyl acetate,



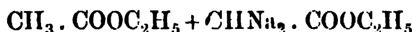
$$CH_2Na.COOC_2H_5 \text{ and } CHNa_2.COOC_2H_5$$

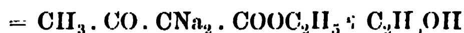
which with ethyl iodide yield ethyl- and diethyl-acetic ester. The formation of ethacetone and diethacetone carbonate of ethyl was explained by the union of a molecule of ethyl acetate with a molecule of mono- or di-sodium acetic ester formed by the action of sodium on acetic ester.





$$CH_3.COOC_2H_5 + CH_2Na.COOC_2H_5 = CH_3.CO.CHNa.COOC_2H_5 + C_2H_5OH$$





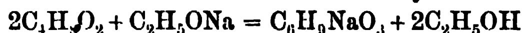
$$CH_3.COOC_2H_5 + CHNa_2.COOC_2H_5 = CH_3.CO.CNa_2.COOC_2H_5 + C_2H_5OH$$

The action of ethyl iodide on the two sodium compounds would produce ethacetone and diethacetone carbonic esters. These views were generally accepted, and the name of Geuther's ethyldiacetic acid was subsequently changed to acetoacetic ester.

But in a subsequent paper [1] Geuther pointed out that he had failed to isolate either the mono- or di-sodium acetic ester ; but had found that a considerable quantity of acetoacetic ester is formed by the

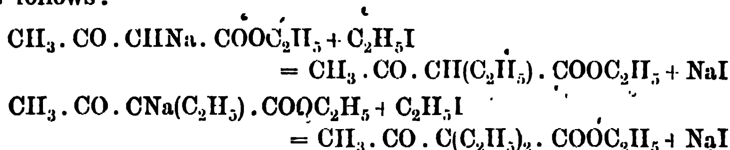
[1] *Zeit. Chem.*, 1868, 652.

action of sodium ethoxide on ethyl acetate, a reaction which he represented as follows:



$$2C_4H_8O_2 + C_2H_5ONa = C_6H_9NaO_3 + 2C_2H_5OH$$

He observed at the same time that when the ethyl derivative of acetoacetic ester is heated with sodium ethoxide, ethyl butyrate is produced. It is therefore unnecessary to assume the formation of the monosodium compound of ethyl acetate, since the presence of sodium ethoxide alone will explain, in accordance with Geuther's original equation, the formation of both acetoacetic ester and ethyl butyrate. The production of diethylacetic ester and diethylacetoacetic ester (Frankland and Duppa's diethacetone carbonate of ethyl) still remained unexplained. In a paper published in 1877 by J. Wislicenus,[1] the whole subject was submitted to a critical re-examination with results which have proved of the highest importance to synthetical organic chemistry. Wislicenus showed that, although only one atom of hydrogen in acetoacetic ester can be replaced by sodium by the direct action of the metal, or of sodium ethoxide, an alkyl group having been introduced in place of this atom of sodium, the compound acquires the property of exchanging a second atom of hydrogen for sodium, which can be replaced by a second alkyl group. Wislicenus, adopting Frankland's formula, represented the changes as follows:



$$CH_3.CO.CHNa.COOC_2H_5 + C_2H_5I = CH_3.CO.CH(C_2H_5).COOC_2H_5 + NaI$$

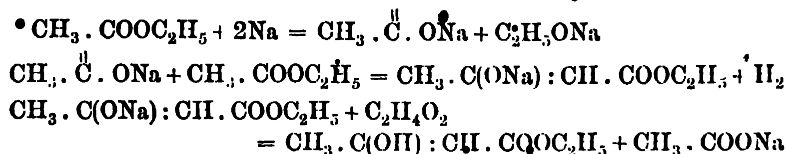
$$CH_3.CO.CNa(C_2H_5).COOC_2H_5 + C_2H_5I = CH_3.CO.C(C_2H_5)_2.COOC_2H_5 + NaI$$

As the second product yields, with sodium ethoxide, diethylacetic ester, Frankland and Duppa's assumption of a disodium acetic ester proved as unnecessary as that of the monosodium compound.

But Wislicenus's inquiry was not limited to unravelling Frankland and Duppa's experiments. The knowledge of the numerous transformations which acetoacetic ester undergoes, the formation of mono- and di-alkyl derivatives, the conditions which determine the ketonic and acid hydrolysis, and the synthetic method for preparing acids and ketones by a combination of the two processes, are due to him, and now belong to the most familiar synthetic reactions in organic chemistry. Although Wislicenus accepted Frankland's formula for acetoacetic ester in opposition to Geuther's, as the most simple explanation of its behaviour, he did not succeed in throwing any new light on the manner in which acetoacetic ester is produced.

[1] *Annalen*, 1877, 186, 163.

Geuther,[1] who regarded both the sodium compound and the free ester as possessing the hydroxyl, or, as we now say, the enolic structure, explained the process in the following manner :

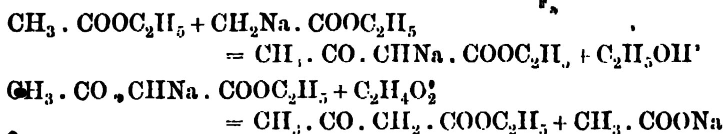


$$CH_3.COOC_2H_5 + 2Na = CH_3.\overset{\|}{C}.ONa + C_2H_5ONa$$

$$CH_3.\overset{\|}{C}.ONa + CH_3.COOC_2H_5 = CH_3.C(ONa):CH.COOC_2H_5 + H_2$$

$$CH_3.C(ONa):CH.COOC_2H_5 + C_2H_4O_2 = CH_3.C(OH):CH.COOC_2H_5 + CH_3.COONa$$

Frankland and Duppa,[2] on the other hand, represented the reaction as due to the formation of a sodium compound of acetic ester, which then united with a second molecule of acetic ester,

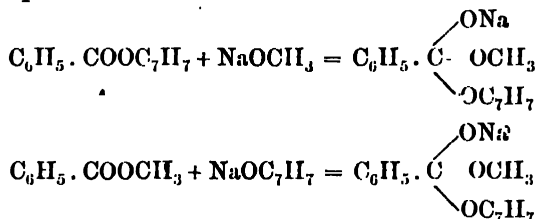


$$CH_3.COOC_2H_5 + CH_2Na.COOC_2H_5 = CH_3.CO.CHNa.COOC_2H_5 + C_2H_5OH$$

$$CH_3.CO.CHNa.COOC_2H_5 + C_2H_4O_2 = CH_3.CO.CH_2.COOC_2H_5 + CH_3.COONa$$

The controversy which the structure of acetoacetic ester aroused, and out of which the theory of tautomerism was ultimately evolved (Part II, chap. vi), diverted attention for a time from the mechanism of the reaction. In the meanwhile, Frankland's ketonic formula for both the free ester and sodium compound, which expressed in a simple fashion the greater number of its transformations, was generally accepted.

The first serious contribution to a theory of the acetoacetic ester synthesis is contained in a paper by Claisen[3] published in 1887, in which he shows that benzyl benzoate unites with sodium methylate and methyl benzoate with sodium benzylate to form the same additive compound.



$$C_6H_5.COOC_7H_7 + NaOCH_3 = C_6H_5.C\begin{cases}ONa\\OCH_3\\OC_7H_7\end{cases}$$

$$C_6H_5.COOCH_3 + NaOC_7H_7 = C_6H_5.C\begin{cases}ONa\\OCH_3\\OC_7H_7\end{cases}$$

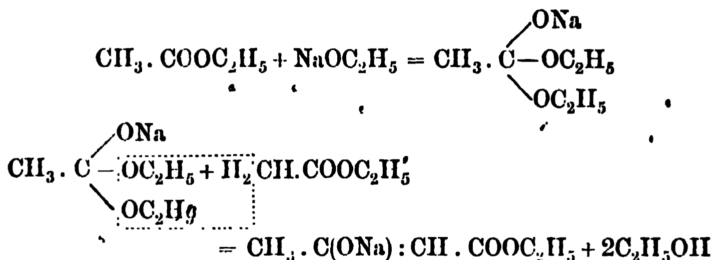
Benzaldehyde also produces the same substance by the action of sodium methylate.



$$2C_6H_5.CHO + NaOCH_3 = C_6H_5.C(OCH_3)(OC_7H_7)(ONa)$$

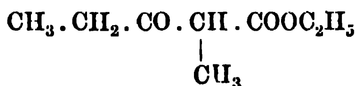
[1] *Annalen*, 1883, 219, 123.
[2] *Phil. Trans.*, 1866, 156, 37 ; *Annalen*, 1866, 138, 204, 328.
[3] *Ber.*, 1887, 20, 646.

On the basis of this observation, Claisen suggested that acetoacetic ester is produced in two stages. A molecule of sodium ethoxide unites with ethyl acetate and forms an additive compound, the latter combining with a second molecule of ethyl acetate to form sodium acetoacetic ester, with the elimination of two molecules of alcohol.

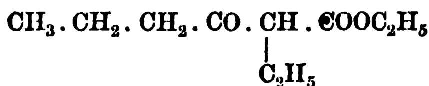


According to Claisen, therefore, the active agent in the process is not metallic sodium, but sodium ethoxide. This view received support from a variety of independent observations. Ladenburg in 1870 made the interesting discovery that ethyl acetate, carefully freed from alcohol by means of silicon chloride, is not attacked by sodium in the cold, and only very slowly on heating. It was also observed that, when ethyl acetate only contains a trace of alcohol, the action of sodium at the commencement is very slow, but increases in vigour as it proceeds, a fact which Claisen ascribed to the liberation of constantly increasing quantities of alcohol, as expressed in his equation. Moreover, Claisen's theory explained the enolic structure of the sodium compound, which was by this time generally recognized. But the most convincing proof of the active agency of sodium ethoxide was afforded by the large number of similar condensations effected between different esters or between esters and ketones either with alcohol-free sodium ethoxide, or, less frequently, with an alcoholic solution of sodium ethoxide in place of metallic sodium.

Some of these reactions will now be illustrated. It may be stated at the outset that the number of condensations effected with sodium ethoxide far exceeds that with metallic sodium. Acetic ester, however, gives a very much better yield with sodium than with sodium ethoxide, which even at 170° only produces about one-third of the theoretical amount. Sodium acts similarly with propionic and butyric ester, but with much diminished yields. These products of these two reactions have the structure,

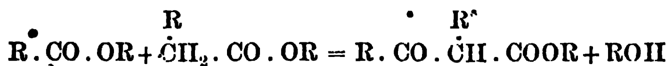


Propiopropionic ester.

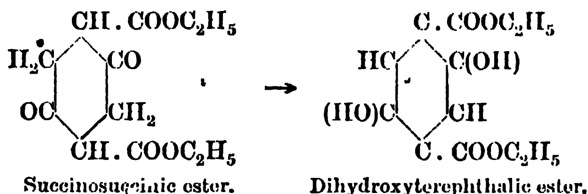


Butyrobutyric ester.

It follows, therefore, that the carbonyl group of the one ester molecule attaches itself to the α-carbon of the second, and that the reaction may be expressed in the following general form :

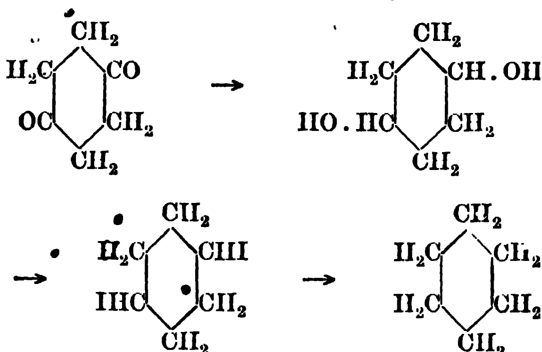


Succinic ester and sodium give the interesting cyclic compound succinosuccinic ester, which on oxidation is easily transformed into dihydroxyterephthalic ester :



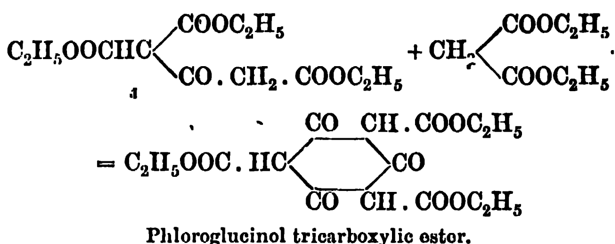
Succinosuccinic ester. Dihydroxyterephthalic ester.

If, however, it is hydrolysed and heated with sulphuric acid, it loses carbon dioxide and gives a cyclic ketone, which may be reduced to the alcohol, converted into the iodide with hydriodic acid, and finally reduced with zinc and acetic acid to cyclohexane.[1]



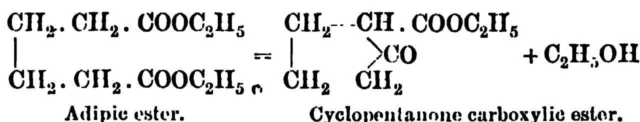
Malonic ester condenses with itself in presence of sodium, giving phloroglucinol tricarboxylic ester, the reaction taking place in two steps.[2]

[1] Baeyer, *Annalen*, 1894, 278, 111.
[2] Baeyer, *Ber.*, 1885, 18, 3454 ; Willstätter, *Ber.*, 1899, 32, 1272.



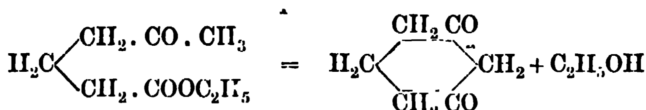
Phloroglucinol tricarboxylic ester.

Other examples of cyclic compounds produced by internal condensation are furnished by the action of sodium on adipic or pimelic esters,[1]

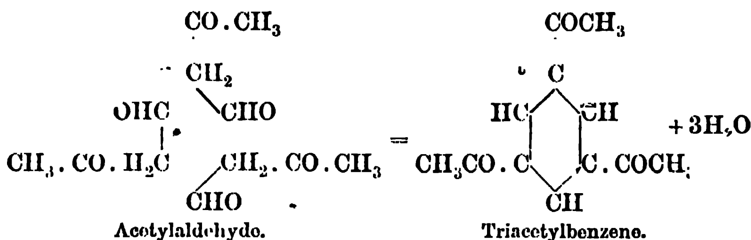


Adipic ester. Cyclopentanone carboxylic ester.

and by the internal condensation of γ-acetobutyric ester which yields dihydroresorcinol.[2]



W. Wislicenus has extended the method to the preparation of aldehyde esters and ketonic-dibasic esters by using formic ester on the one hand and oxalic ester on the other. Acetone and formic ester in presence of sodium ethoxide yield the sodium compound of acetylaldehyde, $CH_3 . CO . CH_2 . CHO$, which, on the addition of acetic acid, almost immediately undergoes further condensation to triacetylbenzene.

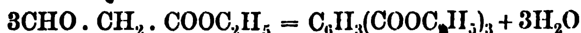


Acetylaldehyde. Triacetylbenzene.

Acetophenone and formic ester can be converted in the same way into tribenzoylbenzene. Formylacetic ester, which is obtained by

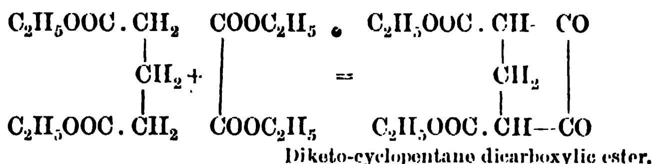
[1] Dieckmann, *Ber.*, 1894, 27, 102.
[2] Vorländer, *Annalen*, 1897, 294, 253.

condensing formic and acetic esters in presence of sodium, rapidly passes into trimesic ester at the ordinary temperature.[1]



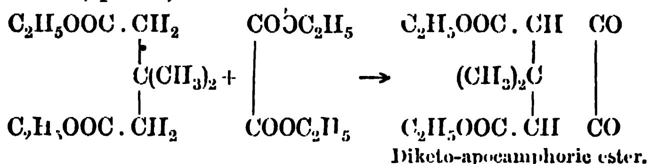
Formylphenylacetic ester, which is prepared with sodium ethoxide from formic and phenylacetic ester, yields two desmotropic forms (Part II, p. 333) but does not undergo further condensation.[2]

Oxalic ester has been a prolific source of new condensation products owing to the ease with which it combines, in consequence no doubt of its acidic character. In some cases an alcoholic solution of sodium ethoxide in place of the alcohol-free substance is sufficient to induce condensation. A variety of ketonic cyclic compounds have been prepared. For example, by condensing glutaric and oxalic ester[3] a derivative of cyclopentane is obtained:



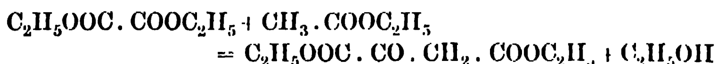
Diketo-cyclopentane dicarboxylic ester.

and by combining $\beta\beta$-dimethylglutaric ester with oxalic ester Komppa[4] synthesised diketoapocamphoric acid and later camphoric acid (Part III, p. 242).

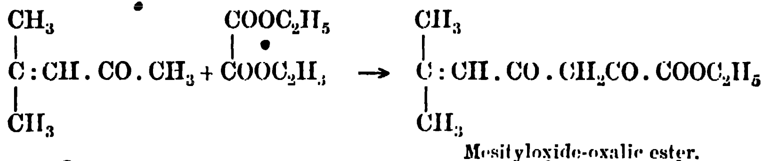


Diketo-apocamphoric ester.

Acetic ester and oxalic ester yield oxaloacetic ester,



With mesityl oxide, oxalic ester gives mesityloxide oxalic ester

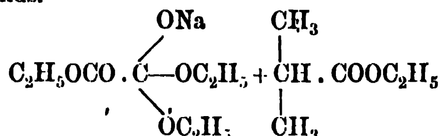


Mesityloxide-oxalic ester.

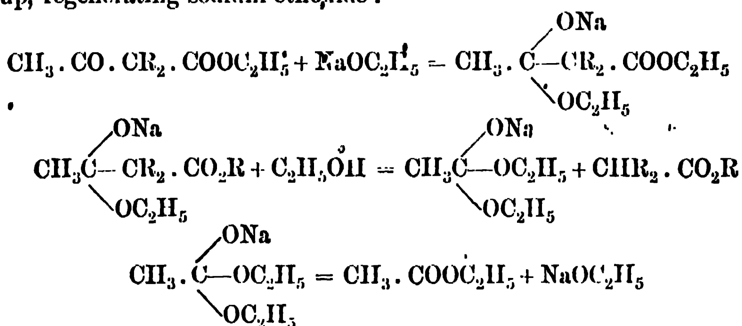
Oxalic ester also readily condenses with propionic and normal butyric ester but not with isobutyric ester.

[1] Piutti, *Ber.*, 1887, 20, 537.
[2] Wislicenus, *Ber.*, 1887, 20, 2930.
[3] Dieckmann, *Ber.*, 1897, 30, 1470.
[4] *Ber.*, 1901, 34, 2472.

In the latter observation Claisen saw a confirmation of his theory, to which we will now return; for the structure of isobutyric ester does not admit of the removal of the two molecules of alcohol which the interaction of the additive compound of oxalic ester with sodium ethoxide demands.



The fact has, however, received a much simpler interpretation from Dieckmann,[1] who has shown that the more acidic the β-ketonic ester, the less readily does it undergo acid hydrolysis with sodium ethoxide. Acetoacetic ester is very slowly hydrolysed at 180° with sodium ethoxide in alcoholic solution and is scarcely affected at the boiling temperature; the monoalkyl esters change somewhat more readily, whilst the dialkyl esters are completely hydrolysed on warming the alcoholic solution containing a trace of sodium ethoxide. The catalytic action of sodium ethoxide is explained by Dieckmann by supposing that a molecule of sodium ethoxide and then a molecule of alcohol are taken up by the ester and that the product then breaks up, regenerating sodium ethoxide:



It is clear, therefore, that the apparently passive character of isobutyric ester is due not so much to its structure as to the instability of the condensation product with oxalic ester. It seems to follow that the process depends in some measure on the acidic character of the final product, or, in other words, on the stability of the sodium compound of the ketonic ester. If this is so, it explains the remarkable differences which have been observed in the effect of the condensing agent, the velocity of the reaction, and the amount of the products.

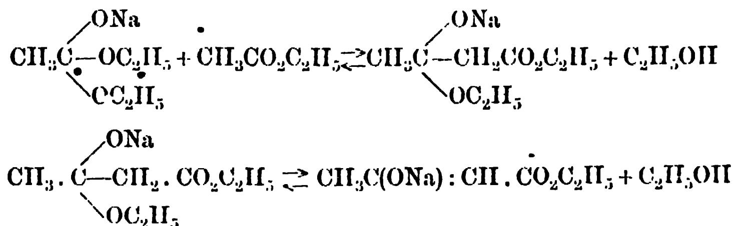
[1] *Ber.*, 1900, 33, 2670.

The sluggish action and unsatisfactory yield obtained with propionic and still more with butyric ester may be due to the more positive character of the product, whilst the readiness with which oxalic ester enters into reactions, especially with other acidic substances like acetophenone, may depend upon the enhanced stability of the sodium compound of the ketonic ester. We are, in fact, dealing with a wide range of reversible reactions in which the balance changes first to one side and then to the other.

We may inquire a little more fully into the mechanism of the changes just described. From what has been stated, one is almost forced to the conclusion that the use of sodium, of dry sodium ethoxide or its alcoholic solution, and latterly of sodamide, to which reference will be made presently (p. 233), only constitutes different modifications of the same fundamental process.

This in itself is a strong argument in favour of Claisen's theory. Claisen has however withdrawn somewhat from his original position. In a recent paper[1] he reaffirms his view of the rôle which sodium ethoxide plays in forming an additive compound, but leaves undetermined the nature of the succeeding changes.

Dieckmann, by reversing the process by which he conceives hydrolysis with sodium ethoxide to be effected, explains the acetoacetic ester synthesis by a series of reversible steps as follows:

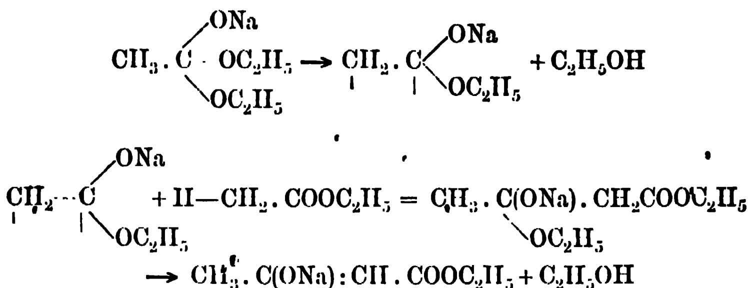


This scheme at first sight does not appear to differ materially from Claisen's original conception; but it implies that the condensation does not necessarily involve both steps, and that in some cases, especially where ring formation is involved, the removal of only one molecule of alcohol may occur and determine the final result.

Claisen's theory, even in its modified form, has not passed unchallenged. Nef[2] explains the acetoacetic ester and many other condensations as due to dissociation of hydrogen from carbon in the negative group of one molecule and the formation of an unsaturated group in the second, under the influence of the specific reagent.

[1] *Ber.*, 1903, 36, 3674; 1905, 38, 709; 1908, 41, 1260.
[2] *Annalen*, 1897, 298, 218.

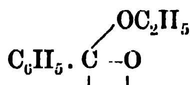
In the present case Claisen's additive compound is supposed to lose alcohol and the unsaturated group in the nascent state to unite with the dissociated acetic ester molecule.



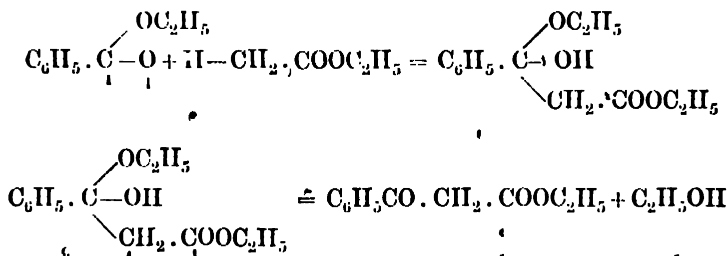
The dissociation is enhanced by the presence of negative atoms and groups, so that compounds containing carbonyl, cyanogen, and nitro groups more easily undergo condensation. Malonic ester, being more negative, dissociates more easily into H and $CH(COOR)_2$ than acetic ester into H and $CH_2 . COOR$.

Those reagents which promote dissociation—acids, alkalis, metals, &c.—assist condensation. The same principle is applied to other condensations.

The formation of benzoylacetic ester, which cannot be well explained by supposing that hydrogen is dissociated from the nucleus in benzoic ester, is brought under a different scheme. Here the unsaturated group is



which unites with acetic ester as follows:



That the same kind of reaction should necessitate such different interpretations seems scarcely satisfactory.

Michael[1] has opposed Claisen's theory for many and various

[1] *J. prakt. Chem.*, 1888 (2), 37, 507; *Ber.*, 1900, 33, 3731; 1905, 38, 1922.

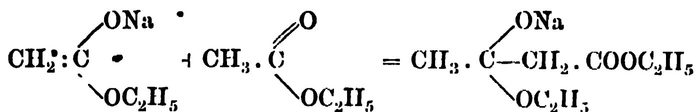
reasons, but chiefly on the ground that no additive compound such as Claisen describes has been isolated; that there is no evidence that it exists; that, moreover, the yield of acetoacetic ester is much diminished by substituting sodium ethoxide for sodium, whereas the reverse would be anticipated.

The formation of such an intermediate additive compound is also out of harmony with his 'neutralisation law'. This law, which is based on energy changes, has already been discussed (p. 113). Michael is perhaps more formidable as a critic than as a theorist, for his own explanation has a weak point, inasmuch as he draws a distinction between the mechanism of the change effected by sodium and that produced by sodium ethoxide. The explanation having reference to sodium is briefly as follows. The sodium, which is rich in positive potential energy, replaces hydrogen in acetic ester and gives rise to the compound $CH_2Na.COOC_2H_5$, which isomerises at once to



$$CH_2:C(ONa)OC_2H_5;$$

but the positive energy of the sodium is still unexhausted, and, in the next phase, the sodium acetic ester, which still possesses free positive energy, seizes on the carbonyl group of acetic ester, containing free negative energy, whereby the metal is so far neutralised that further condensation stops.

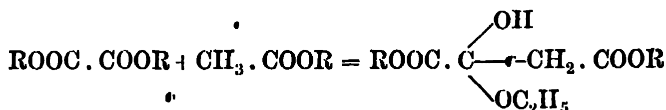


$$CH_2:C\begin{matrix}\nearrow ONa \\ \searrow OC_2H_5\end{matrix} + CH_3.C\begin{matrix}\nearrow\!\!\!\!\nearrow O \\ \searrow OC_2H_5\end{matrix} = CH_3.C\begin{matrix}\nearrow ONa \\ \searrow OC_2H_5\end{matrix}\!\!-CH_2.COOC_2H_5$$

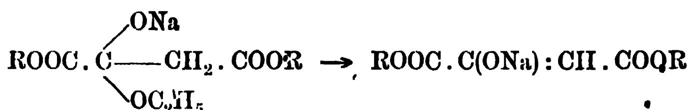
Finally, a molecule of alcohol is detached. The above change cannot be effected by sodium ethoxide, as it possesses less free energy than metallic sodium.

It will be seen that so far as the acetoacetic ester synthesis is concerned there is no essential difference between the views of Michael and Nef. According to Michael, where sodium ethoxide is used, a process of polymerisation similar to the aldol condensation is induced (see p. 237). This condensation is brought about by the free energy of the carbonyl group in the one molecule and the mobility of the hydrogen atom, due to the proximity of a negative group in the other molecule. Thus, the union of acetic and oxalic ester will be formulated as follows:

[1] *J. prakt. Chem.*, 1888 (2), 37, 507; 1899 (2), 60, 286, 409.
[2] *Ber.* 1900, 33, 3731; 1905, 38, 1922.



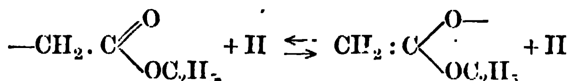
The product then interacts with sodium ethoxide and a molecule of alcohol is finally detached.



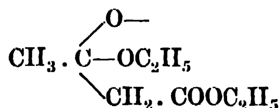
In the acetoacetic ester synthesis the sodium compound is formed previous to condensation; in the oxaloacetic ester it takes place after condensation.

A very ingenious and suggestive explanation of this and other condensations has been advanced by Lapworth.[1] Lapworth supposes that the substance undergoes ionisation, forming an equilibrium mixture of ions.

Acetic ester will yield the following ions:



The presence of a base, by diminishing the concentration of the hydrogen ions, will increase that of the negative ions and accelerate the change. The first represents the negative ion of an organo-metallic compound. Being a weak ion it is capable, by reason of its electro-affinity, of uniting with a neutral component,[2] i.e. a molecule of acetic ester, and of a new complex negative ion thus:



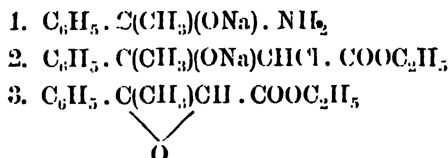
The process may be compared with that by which the alkyl group of a magnesium alkyl halide attaches itself to the carbon of a carbonyl group. The process being reversible, as Dieckman has shown (p. 229), the ion may lose its neutral component and break up into two molecules of acetic ester, or it may form a neutral substance with a positive ion, such as sodium, or it may lose the negative ion, $—OC_2H_5$, in the form of alcohol, and give acetoacetic ester.

[1] *Trans. Chem. Soc.*, 1901, 79, 1269; 1902, 81, 1512; *Proc. Chem. Soc.*, 1903, 19, 190.

[2] See Abegg and Bodländer, *Zeit. anorg. Chem.*, 1899, 20, 475.

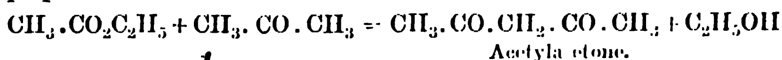
Lapworth has shown the close analogy existing between the aceto-acetic ester condensation and the Grignard and Reformatsky reactions by condensing oxalic ester and bromacetic ester in presence of zinc or magnesium, in the manner already referred to on p. 218.

Before concluding the subject of the acetoacetic ester synthesis reference should be made to the introduction by Claisen of sodamide as a condensing agent.[1] In the majority of cases its action is quieter and more regular than either sodium or sodium ethoxide. It can be used in the synthesis of 1.3 diketones and for alkylating ketones. Acetophenone and ethyl iodide in presence of sodamide give ethyl-acetophenone. By the action of ethyl chloracetate on ketones, glycide esters are formed. The latter reaction is explained by Claisen as proceeding in three phases. In the first an additive compound with sodamide is formed, which undergoes condensation with the ethyl chloracetate and is followed by the removal of sodium chloride.



Modified Acetoacetic Ester Synthesis ($—COOC_2H_5 + CH_2X$; $X = CO, CN$, &c.). It is not essential that the second member taking part in the above condensation process should also be an ester. The place of carbethoxyl may be taken by a variety of negative groups, such as CO in aldehydes and ketones and CN in methyl cyanide and its derivatives. The following examples will illustrate these modifications.

By combining acetic ester with acetone, acetylacetone may be prepared.



Benzoic ester and acetone form benzoylacetone.



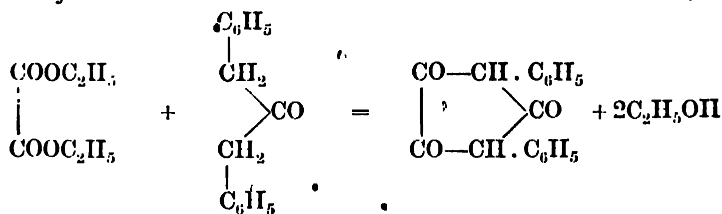
Benzoylacetophenone (dibenzoylmethane) is formed in a similar manner from benzoic ester and acetophenone.



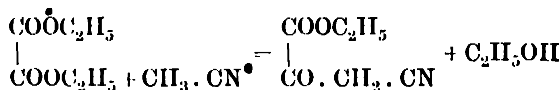
A variety of other compounds have been obtained by Claisen in a similar way.

[1] *Ber.*, 1905, 38, 693.

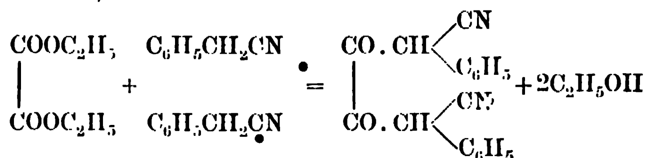
Ring formation is illustrated by the linking of oxalic ester with dibenzyl ketone.[1]



Oxalic ester also condenses in presence of sodium ethoxide with methyl cyanide[2] and benzyl cyanide,[3] the first reaction taking place as follows:

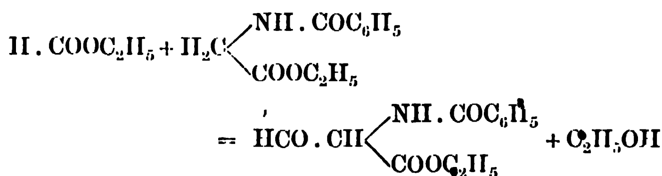


and the second,



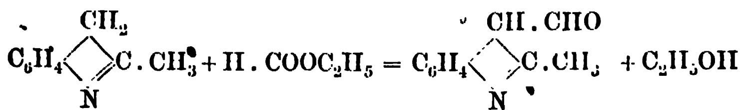
but the most interesting reactions of this type are those in which formic ester is employed.

W. Wislicenus[4] was the first to combine formic ester with ketones, and obtained with acetone and acetophenone the formyl derivatives already referred to (p. 226). Formic ester also combines with hippuric ester,[5]

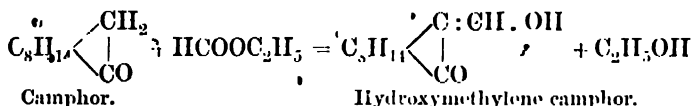


and with methyl indole, in which the CH_2 group derives its negative character from the proximity of the double bond.[6]

[1] Claisen, *Ber.*, 1894, 27, 1353.
[2] Fleischhauer, *J. prakt. Chem.*, 1893, 47, 44.
[3] Volhard, *Annalen*, 1894, 282, 4.
[4] See also Claisen, *Annalen*, 1894, 281, 300.
[5] Erlenmeyer, *Ber.*, 1902, 35, 3769.
[6] Angeli and Marchetti, *Atti R. Accad. Lincei*, 1908, 16, 790.



Condensations with 1, 3-Diketones, Claisen's Method. In studying the action of formic ester on camphor in presence of sodium alcoholate, Claisen[1] obtained *hydroxymethylene camphor.*

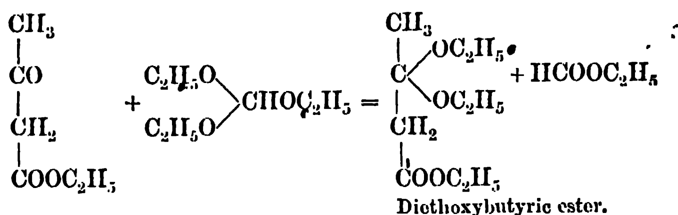


The condensation product possesses strongly acid properties and forms salts and esters after the manner of acids.



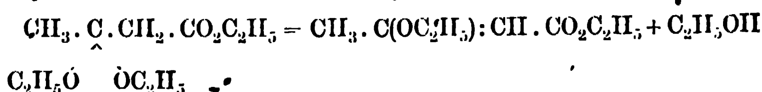
With acetic anhydride and benzoyl chloride it yields an acetyl and benzoyl derivative. But the most significant reactions occur with phosphorus trichloride and the bases, ammonia, aniline and methylaniline. In the first case the hydroxyl is replaced by chlorine, in the second, by the radicals of the three basic groups forming amides. It follows, therefore, that the new carbon group contains hydroxyl, and since it can only be represented by the unsaturated group $=CH(OH)$, the term *hydroxymethylene* has been given to it. The results of this research led to the discovery of other hydroxymethylene compounds possessing still more marked acid properties. By the action of acid chlorides on acetoacetic ester or its metallic compounds the acyl group may replace hydrogen either in the methylene group of the keto form, or in the hydroxyl group of the enol form.[2] Since no acid chloride of formic acid exists, the simplest of the acyl derivatives, namely formylacetoacetic ester, could not be obtained in this way. Formic ester, which might be employed as a substitute for the acyl chloride, does not condense with acetoacetic ester in presence of sodium ethoxide, owing no doubt to the formation of the sodium compound of acetoacetic ester, which would inhibit any further reaction. This suggested the use of orthoformic ester, but this substance in presence of acetyl chloride condenses in the following unexpected fashion, giving diethoxybutyric ester.[3]

[1] *Annalen*, 1894, **281**, 306.
[2] The replacement of the radical in the hydroxyl of the enol form is best accomplished by means of the acyl or alkyl halide in presence of pyridine.
[3] *Ber.*, 1893, **26**, 2729.

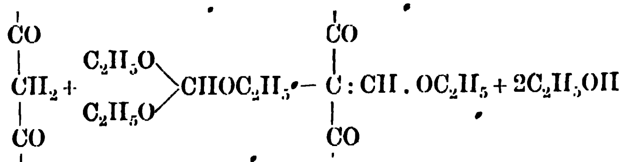


Diethoxybutyric ester.

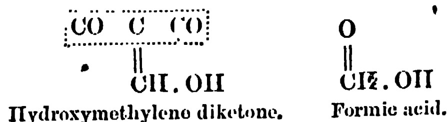
The latter, on distillation, loses a molecule of alcohol and forms ethoxycrotonic ester, the isomer of ethylacetoacetic ester.



If, however, acetic anhydride is employed as condensing agent, the following reaction occurs, which is shared by other 1.3 diketones, such as malonic ester, acetylacetone, &c.[1]

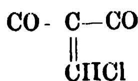


These substances represent esters of strong monobasic acids, for they are hydrolysed by either water or alkalis yielding the free acid or its salt, and are converted into amides by ammonia or amines. The strength of the acids, as determined from their electrical conductivities, is of the order of acetic acid. Claisen concludes that the group CO—C—CO, which is present in these substances, may play the part of the =O atom in a carboxylic acid, a view which is readily understood by a comparison of the two atomic groupings, the dotted line enclosing the equivalent of the doubly linked oxygen in formic acid.



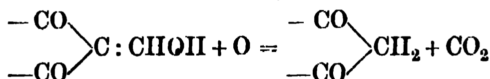
Hydroxymethylene diketone. Formic acid.

The presence of the hydroxymethylene group in these compounds is proved, as in hydroxymethylene camphor, by the action of phosphorous chloride, which removes hydroxyl, giving the acid chloride.



[1] *Annalen*, 1897, 297, 1.

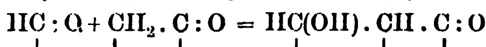
On heating the latter with the sodium salt of the acid, a compound having all the characteristics of an anhydride is produced. The free acids rapidly absorb oxygen and, on warming, evolve carbon dioxide, when the original diketone is regenerated.



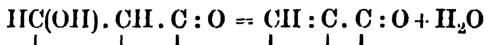
The compounds undergo various other interesting changes, for an account of which the original paper must be consulted.

The use of aldehydes and ketones as participating members in a condensation introduces a whole series of closely related reactions, among which are included the aldol condensation, Claisen's reaction, and the benzoin condensation. These reactions can only be treated in a very general way. It should be noted that although the mechanism of the change is probably closely related to that of the acetoacetic ester synthesis and allied reactions, the result in the majority of cases is essentially different, inasmuch as it leads indirectly to the separation of water and the formation of a double bond between the newly attached carbon atoms.

The Aldol Condensation ($CO + CH_2 . CO$). This condensation, which was discovered by Wurtz,[1] occurs between aldehydes and ketones, and may be expressed by the following general scheme:



A second phase in the process results in the elimination of water and the production of an unsaturated compound.



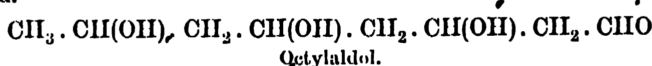
The first is the aldol, the second the crotonaldehyde condensation. Sometimes the first phase does not appear and only the second becomes manifest.

The usual reagents, which effect the condensation, are hydrochloric acid, potassium carbonate, potassium cyanide or caustic soda solution, and less frequently sulphuric acid, acetic acid, acetic anhydride, and zinc chloride.

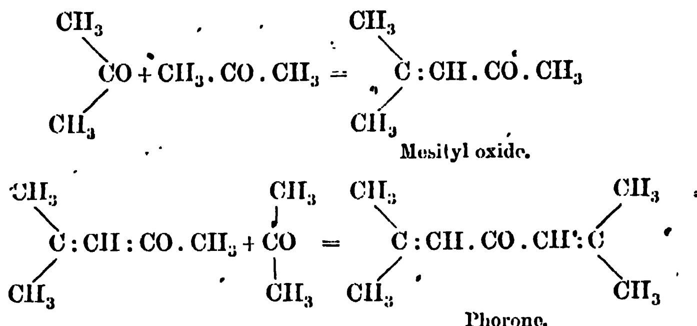
The type of all these condensations is the formation from acetaldehyde of aldol (hydroxybutylaldehyde) and crotonic aldehyde. The first reaction occurs in presence of hydrogen chloride or potassium carbonate, and the second either by the action of heat on the aldol, or by the direct action of zinc chloride on acetaldehyde. Aldol

[1] *Jahresb.*, 1872, 449.

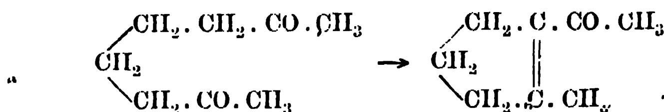
will condense again with itself, giving normal octylaldol, as Raper found.[1]



The production of mesityl oxide and phorone by the action of hydrogen chloride on acetone[2] is another example of the crotonaldehyde condensation.

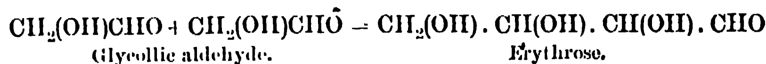


The reaction has also been used for preparing unsaturated cyclic compounds. Diacetylbutane and strong sulphuric acid yield methylcyclopentene methyl ketone.[3]



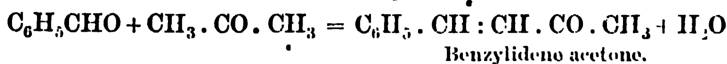
Diacetylpentane gives in the same way methyltetrahydrobenzene methyl ketone.[4]

Claisen's Reaction. A special interest attaches to the use of dilute sodium hydroxide solution as condensing agent, which was first employed by Schmidt[5] and afterwards studied by Claisen.[6] Condensations between aldehydes and a variety of aldehydes and ketones have been effected by this reagent. The syntheses of erythrose from glycollic aldehyde and fructose from glycerose furnish examples of this process (Part III, p. 6).

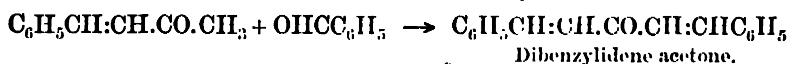


[1] Raper, *J. Amer. Chem. Soc.*, 1907, 91, 1831.
[2] Baeyer, *Annalen*, 1866, 140, 297.
[3] Marshall and Perkin, *Trans. Chem. Soc.*, 1890, 57, 241.
[4] Kipping and Perkin, *Trans. Chem. Soc.*, 1890, 57, 14.
[5] *Ber.*, 1880, 13, 2342.
[6] *Ber.*, 1881, 14, 2471.

In many cases the aldol phase is lost, and only the second phase appears. Claisen found that benzaldehyde and acetone in presence of sodium hydroxide solution (10 per cent.) yield benzylidene and dibenzylidene acetone.

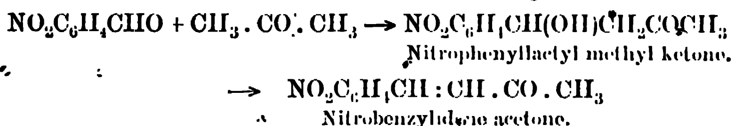


$$C_6H_5CHO + CH_3.CO.CH_3 = \underset{\text{Benzylidene acetone.}}{C_6H_5.CH:CH.CO.CH_3} + H_2O$$



$$C_6H_5CH:CH.CO.CH_3 + OHCC_6H_5 \longrightarrow \underset{\text{Dibenzylidene acetone.}}{C_6H_5CH:CH.CO.CH:CHC_6H_5}$$

With *o*-nitrobenzaldehyde and acetone, Baeyer and Drewsen[1] succeeded in arresting the action at the first stage and obtained the nitrophenyllactyl methyl ketone, which by boiling with acetic anhydride is converted into the unsaturated compound.

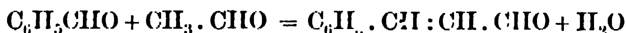


$$NO_2C_6H_4CHO + CH_3.CO.CH_3 \longrightarrow \underset{\text{Nitrophenyllactyl methyl ketone.}}{NO_2C_6H_4CH(OH)CH_2COCH_3}$$

$$\longrightarrow \underset{\text{Nitrobenzylidene acetone.}}{NO_2C_6H_4CH:CH.CO.CH_3}$$

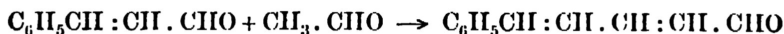
In this condensation an excess of alkali is to be avoided, otherwise indigo is formed.

If the new compound obtained by means of this reaction is an aldehyde, like cinnamic aldehyde (which is formed from benzaldehyde and acetaldehyde), the process of condensation may be repeated.



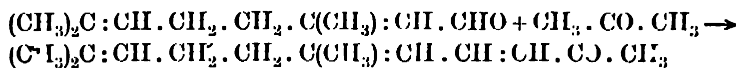
$$C_6H_5CHO + CH_3.CHO = C_6H_5.CH:CH.CHO + H_2O$$

As Einhorn and Diehl[2] have shown, cinnamic aldehyde may undergo a second condensation with another molecule of acetaldehyde or acetone.



$$C_6H_5CH:CH.CHO + CH_3.CHO \longrightarrow C_6H_5CH:CH.CH:CH.CHO$$

This method of condensation has received an interesting technical application in the preparation of *ionone*—a substitute for essence of violets, the sweet-smelling principle of which it closely resembles both in structure and perfume. Ionone was prepared by Tiemann and Krüger[3] from citral, an aldehyde contained in citron and lemon-grass oil (Part III, p. 257). Citral and acetone condense in presence of baryta solution to form *pseudo-ionone*, which is converted in turn into a mixture of α- and β-ionone on boiling with sulphuric acid.

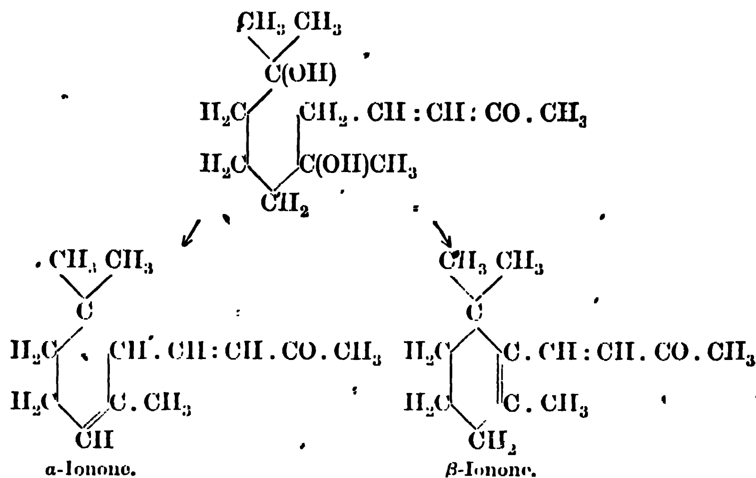


$$(CH_3)_2C:CH.CH_2.CH_2.C(CH_3):CH.CHO + CH_3.CO.CH_3 \longrightarrow$$
$$(CH_3)_2C:CH.CH_2.CH_2.C(CH_3):CH.CH:CH.CO.CH_3$$

The conversion of pseudo-ionone into α- and β-ionone may be sup-

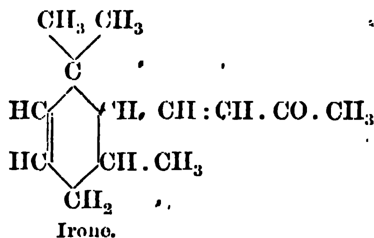
[1] *Ber.*, 1882, 15, 2857. [2] *Ber.*, 1885, 18, 2320. [3] *Ber.*, 1898, 31, 808.

posed to take place by the addition and subsequent removal of two molecules of water.



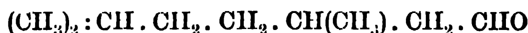
α-Ionone. β-Ionone.

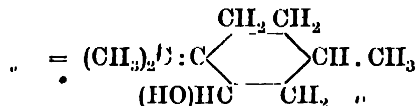
Irone, the perfume itself, is represented by the formula[1]



Irone.

Another example of cyclic formation is furnished by the conversion of citronellal into isopulegol.[2]

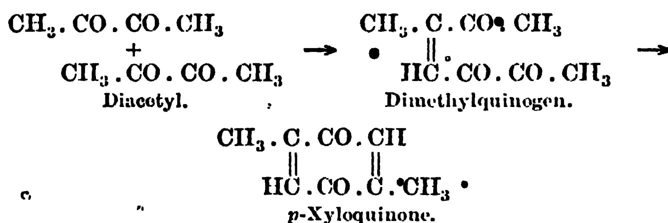




Like the aldehydes, diketones may undergo condensation with other ketones, and Japp[3] and others have succeeded in forming products by combining benzil and phenanthraquinone with acetone, &c. An interesting application of the same reaction is due to von Pechmann,[4] who prepared quinones of the benzene series by a similar process.

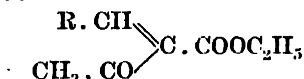
[1] *Ber.*, 1891, **26**, 2675.
[2] Tiemann and Schmidt, *Ber.*, 1896, **29**, 913.
[3] *Ber.*, 1883, **16**, 275, 282.
[4] *Ber.*, 1888, **21**, 1417; 1895, **28**, 1845.

Thus, diacetyl and sodium hydroxide gave first the intermediate product *dimethylquinogen* and by internal condensation p-*xyloquinone*.



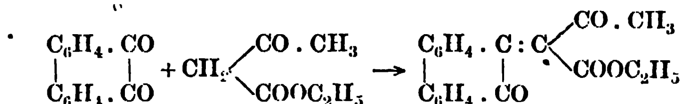
Acetyl propionyl forms, in the same way, duroquinone.

Knoevenagel's Reaction ($CO + CH_2X$; X = CO ; CN ; NO_2, &c.). Among the earlier attempts to bring about condensation of aldehydes and ketones with 1 . 3 diketones and ketonic esters is that of Claisen,[1] who, by the use of hydrogen chloride, succeeded in obtaining condensation products with acetaldehyde, benzaldehyde, and acetoacetic ester of the formula :

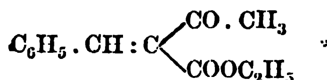


Much more effective reagents for this purpose are ammonia and the primary and secondary bases, and even glycocoll and other amino acids can be used in some cases.[2]

Japp and Streatfeild[3] were the first to employ ammonia to condense phenanthraquinone and acetoacetic ester.

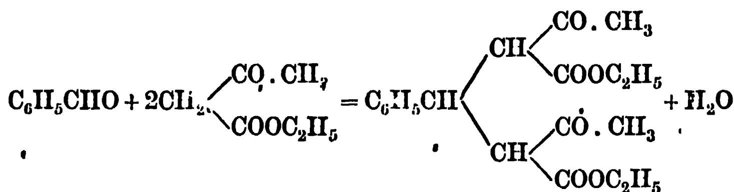


In 1893 Knoevenagel[4] carried out a much more complete investigation, in which not only ammonia, but diethylamine, piperidine and aniline were used with success. Thus, benzaldehyde, in presence of small quantities of diethylamine, condenses with acetoacetic ester when cooled in a freezing mixture, forming benzylidene acetoacetic ester, that is, the compound which Claisen obtained with hydrogen chloride.

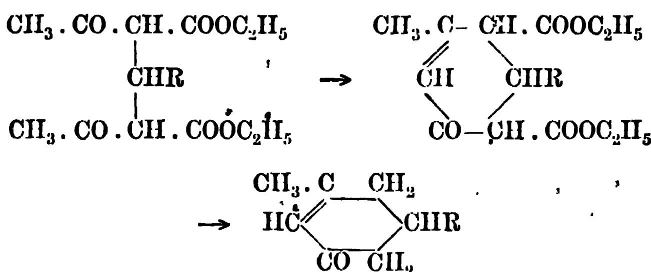


[1] *Annalen*, 1883, 218, 172. [2] Dakin, *Journ. Biol. Chem.*, 1909, 7, 49.
[3] *Trans. Chem. Soc.*, 1883, 43, 27.
[4] *Annalen*, 1894, 281, 25 ; *Ber.*, 1904, 37, 446.

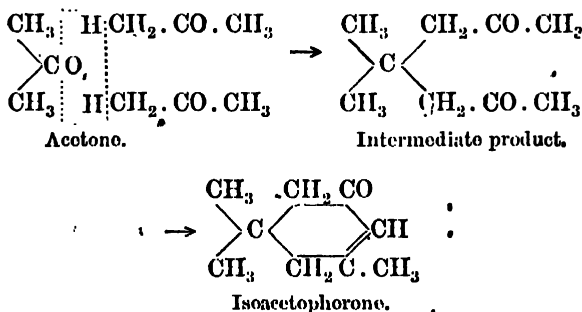
In some cases two molecules of the 1.3 diketone condense with the aldehyde if the process is conducted under modified conditions. Thus, benzaldehyde and acetoacetic ester condense in presence of diethylamine, if the reaction proceeds at the ordinary temperature, to form benzylidenediacetoacetic ester.



Compounds of this character, which may be described as 1.5 diketones, are capable of internal condensation in presence of alkalis or hydrochloric acid, and a variety of cyclic compounds have been built up in this manner, of which the following is an example.[1] Alkylidenediacetoacetic ester undergoes inner condensation with alcoholic potassium hydroxide, and, on hydrolysis, loses carbon dioxide and yields the cyclohexenone derivative.



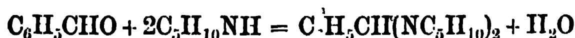
An analogous reaction to the above is the formation of isoacetophorone from acetone and lime.



Isoacetophorone.

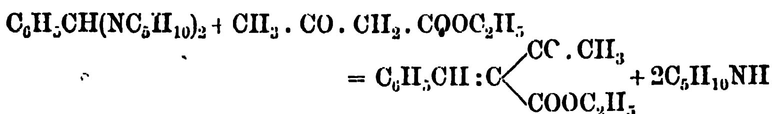
[1] *Annalen*, 1894, 281, 25; 1895, 288, 321.

Knoevenagel explains the action of the condensing agent on the assumption that the aldehyde first unites with the base. Benzaldehyde and piperidine combine as follows :



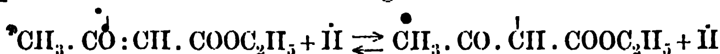
$$C_6H_5CHO + 2C_5H_{10}NH = C_6H_5CH(NC_5H_{10})_2 + H_2O$$

The product then interacts with the diketone and regenerates the base, which thus plays the part of a catalyst.



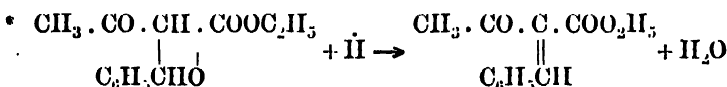
$$C_6H_5CH(NC_5H_{10})_2 + CH_3.CO.CH_2.COOC_2H_5 = C_6H_5CH:C\begin{cases}CO.CH_3\\COOC_2H_5\end{cases} + 2C_5H_{10}NH$$

Another explanation based on ionisation (p. 232) has been advanced by Hann and Lapworth,[1] in which the acetoacetic ester forms an equilibrium mixture of the following ions :



$$CH_3.\overset{\bullet}{C}O:CH.COOC_2H_5 + \overset{\bullet}{H} \rightleftarrows CH_3.CO.\overset{\bullet}{C}H.COOC_2H_5 + \overset{\bullet}{H}$$

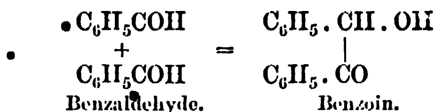
The latter would then combine with the molecule of benzaldehyde as neutral component (see p. 232) from which, by elimination of a hydroxyl ion, benzylidene-acetoacetic ester would be produced.



$$\begin{matrix}CH_3.CO.CH.COOC_2H_5\\ | \quad | \\ C_6H_5CHO\end{matrix} + \overset{\bullet}{H} \longrightarrow \begin{matrix}CH_3.CO.C.COOC_2H_5\\ \| \\ C_6H_5CH\end{matrix} + H_2O$$

The effect of the base might be to remove hydrogen ions by forming the complex $NRRH_2$ or introduce hydroxyl ions and thus increase the concentration of the organic ions.

Benzoin Condensation. The action of potassium cyanide on aromatic aldehydes is a peculiar one, and may be represented by the oldest example—the formation of benzoin from benzaldehyde and alcoholic potassium cyanide—which was first studied by Liebig and Wöhler.[2]



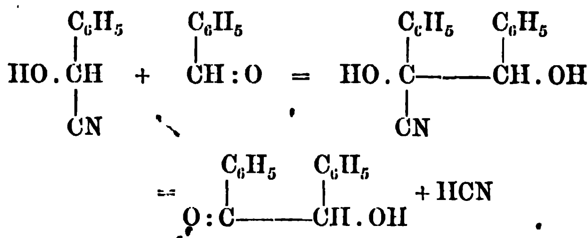
$$\begin{matrix}C_6H_5COH\\+\\C_6H_5COH\end{matrix} = \begin{matrix}C_6H_5.CH.OH\\ | \\ C_6H_5.CO\end{matrix}$$

Benzaldehyde. Benzoin.

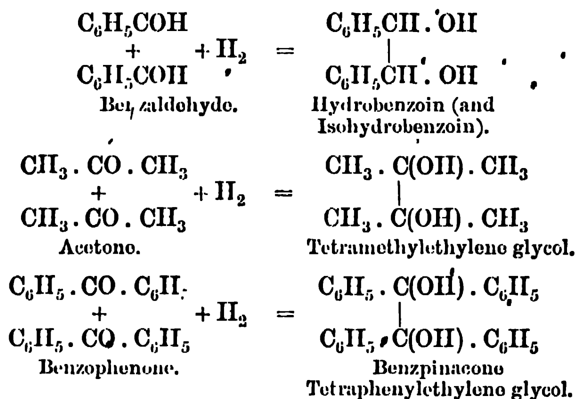
The reaction bears a close resemblance to the aldol condensation. The specific action of the cyanide, which differs fundamentally from that of the caustic alkalis or sodium ethoxide (which produce benzyl benzoate or a mixture of benzyl alcohol and benzoic acid), has received various explanations,[3] the most plausible of which is that

[1] *Trans. Chem. Soc.*, 1904, 85, 46. [2] *Annalen*, 1832, 3, 276.
[3] Knoevenagel, *Ber.*, 1888, 21, 1316 ; Nef, *Annalen*, 1897, 298, 312.

of Lapworth.[1] He suggests that the benzaldehyde forms a cyanhydrin with potassium cyanide, which then condenses with another molecule of benzaldehyde, hydrogen cyanide being finally eliminated.



Pinacone Condensation. A reaction not unlike that which produces aldol and benzoin, and which was first observed by Fittig,[2] is brought about by the action of neutral, alkaline, and occasionally acid reducing agents on aldehydes and ketones. In addition to primary and secondary alcohols, this reaction gives rise to substances known as *pinacones*. In this reaction the molecules of the original compound become linked by the aldehyde or ketone carbon atom; at the same time two atoms of hydrogen are taken up. The compounds are in fact secondary or tertiary glycols. The following examples will illustrate the process:



The first of the above reactions occurs with aromatic aldehydes and a few of the aliphatic aldehydes[3]; the two latter are alike shared by aliphatic and by aromatic ketones. The reaction has been

[1] *Trans.*, 1903, 83, 995.
[2] *Annalen*, 1858, 110, 26; 1859, 114, 54. The name pinacone has reference to the tabular form of the crystals obtained from acetone (πίναξ = table).
[3] Ciusa, *R. Accad. Lincei*, 1913, 22, 681.

used for internal condensation, as, for example, in the preparation of dimethyldihydroxy-cycloheptane from diacetylpentane.[1]

$$CH_2\begin{cases} CH_2 . CH_2 . CO . CH_3 \\ CH_2 . CH_2 . CO \ CH_3 \end{cases} \rightarrow CH_2\begin{cases} CH_2 . CH_2 . C(OH) . CH_3 \\ \qquad\qquad\quad | \\ CH_2 . CH_2 . C(OH) . CH_3 \end{cases}$$

The reduction is usually effected by sodium amalgam, the aluminium-mercury couple, zinc and acetic acid, or zinc and hydrochloric acid.

No very clear explanation of the mechanism of the process is yet forthcoming. The action of sodium on aldehydes and ketones has been studied by Fittig, Beckmann and Paul, and also by Freer, and may possibly throw some light on the subject. Kane, early in the nineteenth century, found that potassium liberates hydrogen from acetone and forms a compound C_3H_5OK, and more recently Freer[2] stated that he had obtained a similar compound by the action of sodium, to which he assigned the formula $CH_3 . C(ONa) : CH_2$. Fittig's[3] observation that sodium acts upon acetone with the production of a sodium compound of pinacone receives a ready interpretation if we assume that two molecules of a nascent sodium acetone become linked in process of reduction.

$$\begin{array}{c} CH_3 . C(ONa) . CH_3 \\ | \\ CH_3 . C(ONa) . CH_3 \end{array}$$

Beckmann and Paul[4] have shown in the same way that benzaldehyde and benzophenone form sodium compounds which are decomposed by water.

$$\begin{array}{c} C_6H_5COH \\ + \\ C_6H_5COH \\ \text{Benzaldehyde.} \end{array} \begin{array}{c} Na \\ + \\ Na \\ \ \end{array} \rightarrow \begin{array}{c} C_6H_5CH . ONa \\ | \\ C_6H_5CH . ONa \\ \ \end{array} + H_2O \rightarrow \begin{array}{c} C_6H_5CH . OH \\ | \\ C_6H_5CH . OH \\ \text{Hydrobenzoin.} \end{array}$$

$$\begin{array}{c} (C_6H_5)_2CO \\ + \\ (C_6H_5)_2CO \end{array} \begin{array}{c} Na \\ \ \\ Na \end{array} \rightarrow \begin{array}{c} (C_6H_5)_2C . ONa \\ \quad \searrow \\ \qquad > O \\ \quad \nearrow \\ (C_6H_5)_2C . Na \end{array} + H_2O \rightarrow \begin{array}{c} (C_6H_5)_2C . OH \\ | \\ (C_6H_5)_2C . OH \end{array}$$

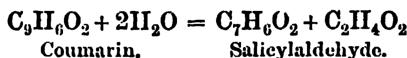
In the latter case benzhydrol is also formed.

According to Schlenk[5] the formula of the sodium compound of benzpinacone has half the molecular weight assigned by Beckmann and Paul, and contains tervalent carbon (p. 65).

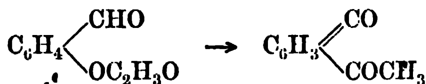
$$\begin{array}{c} | \\ (C_6H_5)_2C . ONa \end{array}$$

[1] Kipping and Perkin, *Trans. Chem. Soc.*, 1891, 59, 214.
[2] *Amer. Chem. J.*, 1893, 15, 582; see also Taylor, *Trans. Chem. Soc.*, 1906, 89, 1258.
[3] *Annalen*, 1859, 110, 25; 1860, 114, 54.
[4] *Annalen*, 1892, 266, 1.
[5] *Ber.*, 1911, 44, 1178.

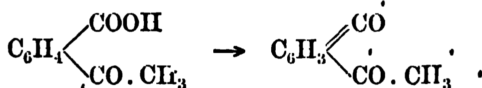
Perkin's Reaction. The history of this interesting reaction dates from Perkin's synthesis of coumarin in the year 1868.[1] Coumarin, the sweet-smelling principle of woodruff and hay, was found to decompose, on fusion with potassium hydroxide, into salicylaldehyde and acetic acid,



from which the natural conclusion was drawn that coumarin was the anhydride of acetylsalicylaldehyde.



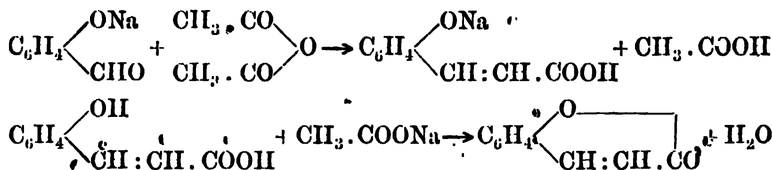
By heating sodium salicylaldehyde with acetic anhydride, coumarin was, in fact, obtained. The evidence seemed conclusive until it was discovered that acetylsalicylaldehyde is unchanged by acetic anhydride, although, with the addition of fused sodium acetate, coumarin is readily produced. The formula assigned by Perkin, which represented coumarin as a derivative of acetylsalicylaldehyde, was disputed by Fittig, who could not reconcile it with the constitution of coumaric acid, of which it is the anhydride; for coumaric acid must then form coumarin by the removal of hydrogen from the benzene nucleus, a process which seemed difficult to reconcile with the properties of the compound.



Fittig preferred to base his view of its constitution on a reaction discovered by Bertagnini[2] for the preparation of cinnamic acid, which consisted in heating benzaldehyde and acetyl chloride.



The formation of coumarin might be explained in an analogous fashion.

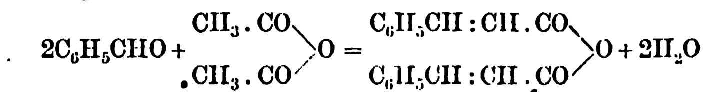


The formula for coumarin as the inner anhydride of *o*-hydroxycin-

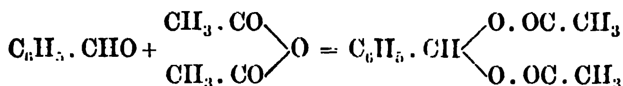
[1] *Trans. Chem. Soc.*, 1868, 21, 53.

[2] *Annalen*, 1856, 100, 126.

namic acid is now universally accepted.[1] In 1877[2] Perkin published a new method for preparing cinnamic acid and analogous compounds by means of a reaction of very general application which now bears his name. It consists in heating a fatty or aromatic aldehyde and the anhydride of a fatty acid, together with its sodium salt, to 180° for several hours. The formation of cinnamic acid from benzaldehyde, acetic anhydride, and sodium acetate was explained by Perkin on the assumption that the anhydride acted upon the aldehyde in the following manner:



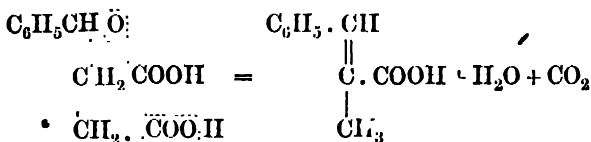
The view was, however, opposed to the observation of Geuther and Hübner, who found that benzaldehyde and acetic anhydride yield benzylidene acetate:



To settle the question, Perkin heated benzaldehyde and acetic anhydride with sodium propionate and obtained cinnamic acid, whereas with propionic anhydride and sodium propionate, phenylcrotonic acid was formed. Perkin assigned to phenylcrotonic acid the formula,



By the interaction of benzaldehyde, succinic anhydride and sodium succinate, a second or isophenylcrotonic acid was subsequently prepared by Perkin, the formation of which received the following interpretation:



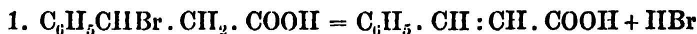
Fittig,[3] who had been engaged in a careful study of the unsaturated acids, was unable to reconcile the properties of the two phenylcrotonic acids with the respective formulae assigned by Perkin. The $\alpha\beta$ unsaturated acids possess the following properties in common: the additive compounds with hydrobromic acid, when heated in

[1] According to Michael (*J. prakt. Chem.*, 1899, 60, 368) Strecker was the first to propose this formula in his *Lehrbuch*.

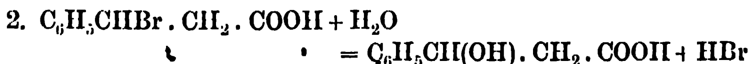
[2] *Trans. Chem. Soc.*, 1877, 32, 389.

[3] *Ber.*, 1894, 27, 2658.

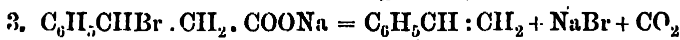
aqueous solution, either lose hydrogen bromide and pass back into the original compound, or the bromine atom is replaced by hydroxyl, whilst in alkaline solution, carbon dioxide and hydrogen bromide are removed, and an unsaturated hydrocarbon results. β-bromo-phenylpropionic acid reacts in the following way:



1. $C_6H_5CHBr.CH_2.COOH = C_6H_5.CH:CH.COOH + HBr$



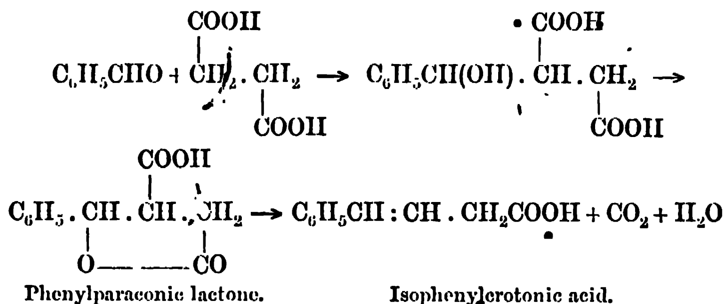
2. $C_6H_5CHBr.CH_2.COOH + H_2O = C_6H_5CH(OH).CH_2.COOH + HBr$



3. $C_6H_5CHBr.CH_2.COONa = C_6H_5CH:CH_2 + NaBr + CO_2$

It was the first and not the second phenylcrotonic acid which behaved in this way and gave with sodium hydroxide solution the unsaturated hydrocarbon, methylstyrene, $C_6H_5CH:CHCH_3$. The two formulae must consequently be reversed. It follows, therefore, that in the reaction between benzaldehyde and propionic acid, it is the α-carbon of the acid which attaches itself to the carbon of the aldehyde group.[1]

In order to follow the phases of the second reaction, Fittig and Jayne[2] repeated Perkin's experiment with benzaldehyde, succinic anhydride, and sodium succinate, but at a temperature of 100° instead of 180°, with the following interesting results: no carbon dioxide was evolved, but phenylparaconic lactone was formed, which, on heating, evolved carbon dioxide and yielded isophenylcrotonic acid. Fittig explained the changes as follows:



$$C_6H_5CHO + \underset{\displaystyle COOH}{\overset{\displaystyle COOH}{CH_2}}.CH_2 \rightarrow C_6H_5CH(OH).\overset{\displaystyle COOH}{CH}.\underset{\displaystyle COOH}{CH_2} \rightarrow$$

$$C_6H_5.\underset{O}{CH}.\overset{COOH}{CH}.\underset{CO}{CH_2} \rightarrow C_6H_5CH:CH.CH_2COOH + CO_2 + H_2O$$

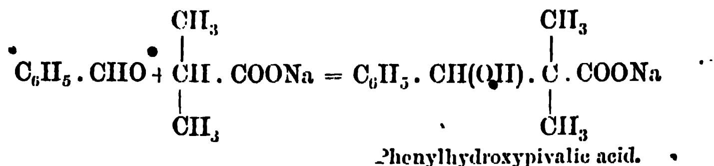
Phenylparaconic lactone. Isophenylcrotonic acid.

The production of a hydroxy compound, which, as in the aldol condensation, Fittig assumed to represent the first phase of the process, was rendered still more probable by the formation of phenyl-hydroxypivalic acid from benzaldehyde and sodium isobutyrate in presence of acetic anhydride.[3]

[1] This view had already found expression in Markownikoff's law, *Annalen*, 1868, 146, 348, and had been further insisted on by Michael (*Ber.*, 1878, 11, 1015).

[2] *Annalen*, 1882, 216, 97.

[3] *Annalen*, 1882, 216, 115.

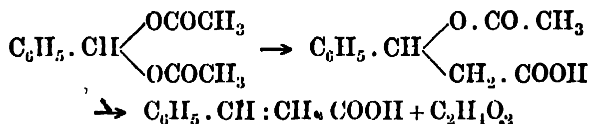


Phenylhydroxypivalic acid.

Fittig found, moreover, that in the preparation of phenylparaconic lactone at the lower temperature, acetic anhydride may replace with advantage succinic anhydride, and this led him to infer that it is the aldehyde and the sodium salt which interact, and not, as Perkin had assumed, the aldehyde and anhydride. By conducting the process at 100° he in fact obtained, from benzaldehyde, sodium propionate and acetic anhydride, phenylcrotonic acid, and from sodium butyrate and acetic anhydride, phenylangelic acid. The fact that Perkin had obtained cinnamic acid from benzaldehyde, acetic anhydride, and sodium propionate now received a simple explanation, for if the reaction is conducted at 100°, the sodium salt of the acid reacts, whereas at 180° double decomposition will occur between the acetic anhydride and sodium propionate or sodium butyrate, yielding sodium acetate and propionic anhydride or butyric anhydride. The sodium salt then produces, with benzaldehyde, cinnamic acid. Fittig's view received apparent confirmation from the experiments of Stuart,[1] who prepared analogous compounds with malonic and isosuccinic acids, both of which are incapable of forming anhydrides. Fittig then drew the following conclusions: Perkin's reaction occurs between the aldehyde and the sodium salt of the acid in two stages; in the first a hydroxy compound is formed, condensation taking place between the aldehyde and α-carbon of the acid; in the second, water is eliminated. In the case of polybasic acids a lactone may be formed from which water and carbon dioxide can be removed on heating. In spite of apparently convincing proofs, Perkin[2] did not relinquish his original view that the interaction takes place between the anhydride and the aldehyde, a view which is also shared by Michael. Perkin pointed out, for example, that the formation of phenylangelic acid on heating a mixture of benzaldehyde, sodium butyrate, and acetic anhydride to 100° does not prove that combination occurs between the aldehyde and the sodium salt; for, in the first place, cinnamic acid cannot be formed under any circumstances at this low temperature, and secondly, the sodium salt and acetic anhydride react readily at 100° to form sodium acetate and butyric anhydride, and the same is true of the salts of other higher fatty acids.[3] Perkin

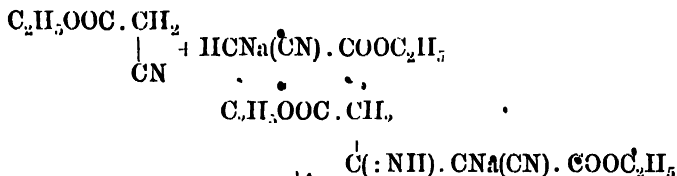
[1] *Ber.*, 1883, 16, 1436. [2] *Trans. Chem. Soc.*, 1886, 47, 317.
[3] Michael, *J. prakt. Chem.* 1899, 60, 364.

suggested that in the preparation of cinnamic acid, the benzylidene diacetate, which is produced by the interaction of benzaldehyde and acetic anhydride, and which is known to decompose into cinnamic acid, may undergo isomeric change and then lose a molecule of acetic acid.

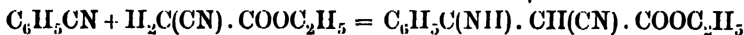


Perkin's theory of the process bears a strong resemblance to that recently suggested by Claisen[1] to explain the acetoacetic ester synthesis. These conflicting results are difficult to adjust, and the question of the course of the reaction must be left for the present undecided.

Thorpe's Reaction. A very different reaction from the foregoing has already been referred to in the introduction to this chapter, namely one involving isomeric change between molecules or parts of a molecule, a reaction which has been introduced and elaborated by Thorpe and his co-workers.[2] To take a simple case, sodium cyanacetic ester combines with cyanacetic ester as follows:



A similar reaction takes place when a cyanogen group is rendered acidic by attachment to a benzene nucleus:



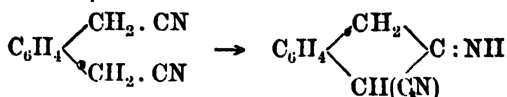
Benzyl cyanide, which may be substituted for the molecule of cyanacetic ester, condenses in presence of sodium ethoxide in a similar fashion:



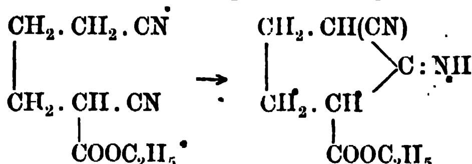
These reactions serve admirably for preparing cyclic structures, provided two cyanogen groups are suitably situated within the molecule.

On heating an alcoholic solution of *o*-xylylene cyanide with a little sodium ethoxide, ring formation at once takes place, with the formation of a cyclopentane ring:

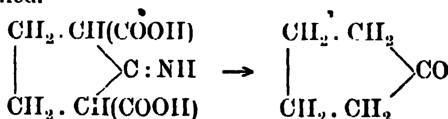
[1] *Ber.*, 1903, 36, 3674; 1905, 38, 709.
[2] *Trans. Chem. Soc.*, 1901, 85, 1726; 1906, 89, 1906; 1907, 91, 578, 1004; 1908, 93, 165.



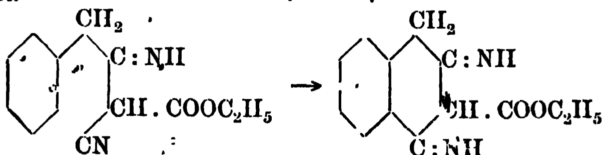
and αδ-dicyanovaleric ester (tetramethylene cyanide not being available for the purpose) gave a corresponding compound.



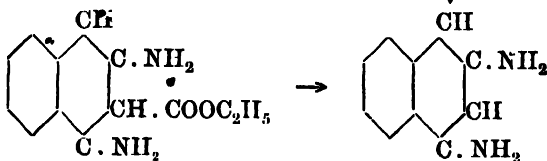
These compounds are readily hydrolysed by heating with dilute sulphuric acid, the C : NH group exchanging NH for oxygen. In the last example hydrolysis converts the cyanogen group into carboxyl, which along with that of the ester group is removed and cyclopentanone is formed.



Naphthalene derivatives have also been obtained by condensing benzyl cyanide with sodium cyanacetic ester and then heating the product.



With concentrated sulphuric acid the latter passes into the diamino-compound and, finally, on hydrolysis of the ester group and heating, into naphthylene-diamine.[1]



REFERENCES.

Die synthetischen Darstellungsmethoden der Kohlenstoff-Verbindungen, by K. Elbs. Barth, Leipzig, 1889.

Synthetische Methoden der organischen Chemie, by T. Posner. Leipzig, 1903.

[1] *Trans. Chem. Soc.*, 1907, 91, 1687; 1909, 95, 261.

Arbeitsmethoden für organisch-chemische Laboratorien, 3rd ed., by Lassar-Cohn. Voss, Hamburg, 1902.

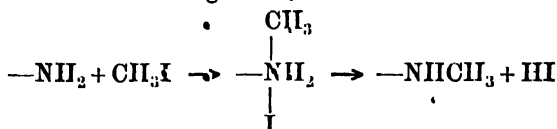
Die Methoden der organischen Chemie, vol. ii, part i, by Th. Weyl. Thieme, Leipzig, 1911.

II. UNION OF CARBON AND NITROGEN

Carbon-Nitrogen Chain Formation. In order to understand the processes underlying ring formation in heterocyclic compounds containing nitrogen, it is desirable to consider first the various reactions which determine the simple linking of carbon and nitrogen. Compared with methods of union of carbon and carbon the number is much more restricted and the attachment generally less stable.

Substitution Methods. It is not always easy to differentiate between reactions effected by replacement and by addition.

1. For example, the action of alkyl iodide on an amino or imino group, which appears to be one of simple substitution, cannot be explained in this way. Nitrogen, being more electronegative than carbon, should attach hydrogen more firmly, nevertheless alkyl halides have no action on paraffins. But if we suppose an additive compound to be first formed and hydrogen iodide then removed, the process becomes more intelligible.



Other reactions leading to the union of carbon and nitrogen by replacement are:

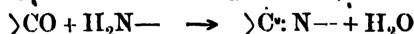
2. The action of acid chlorides on amino- and imino-compounds, giving amides.

3. The action of ammonia and amino compounds on esters with elimination of alcohol, and, in some cases, on acids with separation of water, giving amides.

4. The action of amino- or imino-compounds on unsaturated alcohols (tautomeric diketones and ketonic esters).



5. The action of aldehydes and ketones on amino-compounds and hydrazines, giving unsaturated compounds by removal of water.

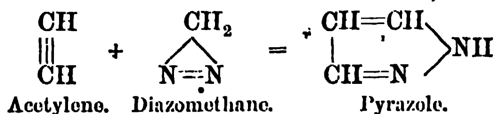


6. The action of nitroso-compounds on the CH_2 group suitably situated.



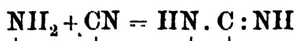
Additive Methods. Among the methods are:

1. Reactions by direct addition of unsaturated compounds, as in the formation of pyrazole from acetylene and diazomethane,

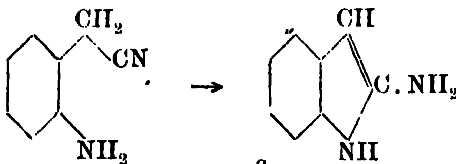


Acetylene. Diazomethane. Pyrazole.

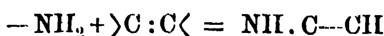
2. Reactions involving intermolecular isomeric change of the following general form:



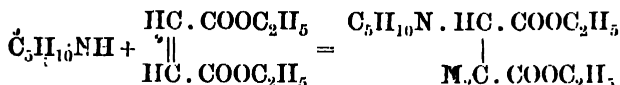
This reaction has been frequently applied in ring formation, as in the case of amino-indole, which is prepared from *o*-amino benzyl cyanide in presence of alkalis;[1]



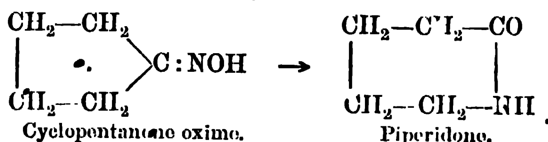
3. Another reaction of the same type is that of the union of a saturated amino-compound with an unsaturated acidic group.



Piperidine combines with fumaric and other unsaturated esters.[2]



4. Intramolecular change effected by Beckmann's reaction (Part II, p. 366), is one which has also been used in ring formation.[3] The oxime of cyclopentanone gives piperidone,



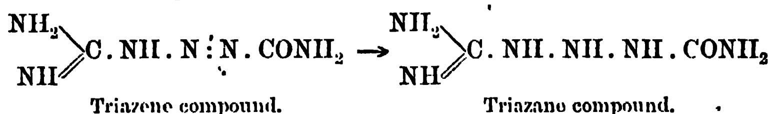
Cyclopentanone oxime. Piperidone.

Stability of Carbon-Nitrogen Chain Formation. The attachment of carbon and nitrogen such as occurs in the case of the amines and amino compounds, in which both atoms are saturated with

[1] Pschorr and Hoppe, *Ber.*, 1910, 43, 581.
[2] Ruhemann, *Trans. Chem. Soc.*, 1898, 73, 723.
[3] Kipping, *Proc. Chem. Soc.*, 1893, 9, 210; Wallach, *Annalen*, 1900, 312, 171; Bamberger, *Ber.*, 1894, 27, 1954, 2795.

hydrogen or hydrocarbon radicals (forming the group $CH_2 . NR_2$) is about as stable as the carbon-carbon union in paraffins. The most drastic treatment will rarely sever the carbon from the nitrogen. This condition is, however, greatly modified if the hydrogen of the CH_2 group is replaced by oxygen. The basic character of the nitrogen is not only greatly weakened, but the new group, $CO . NR_2$, which is characteristic of the class of amides, is readily hydrolysed by alkalis, and the carbon and nitrogen separated, the former as carboxyl and the latter as ammonia or amine. This effect of oxygen in weakening the attachment of the neighbouring atom seems to be common to all chain and ring formations.

The union of unsaturated carbon and nitrogen (RC ⋮ N, RN : C, R_2C : NR) which occurs in such compounds as the cyanides, isocyanides, oximes, hydrazones, &c., is likewise readily severed by hydrolysis with acids. It may be convenient here to draw attention to the nature of the nitrogen-nitrogen combination occurring in carbon compounds. It appears at first sight somewhat remarkable that the union of nitrogen with itself should be so much less stable than that of carbon. Carbon, it is true, is electrochemically more inert than nitrogen, which is the more electronegative element; but it seems scarcely adequate for explaining the fact that a chain of at least sixty carbon atoms may exist in a stable condition in the case of the paraffin hexacontane, $C_{60}H_{122}$, whilst the longest chain of nitrogen atoms saturated with hydrogen or hydrocarbon radicals, so far produced, contains only three nitrogen atoms. The substance in question was obtained with great difficulty by Thiele[1] by the reduction of the corresponding unsaturated triazene compound in the cold, but is of so unstable a character that it decomposes above 0° and could not be isolated in the pure state.



Triazene compound. Triazane compound.

Unsaturated nitrogen chains are much more stable and may be obtained with comparative ease, containing two, three, four, and five atoms of nitrogen, as in the diazo- and the diazoamino-compounds, R . N=N . NH . R, the diazohydrazides, RN=N . N(R) . NH_2, the tetrazones R_2N . N=N . NR_2, and the bis-diazoamino-compounds, obtained by combining two molecules of a diazo-compound with one molecule of ammonia or amine, R . N=N . NH . N=N . R. None are, however, very stable, and all readily decompose with acids or when heated,

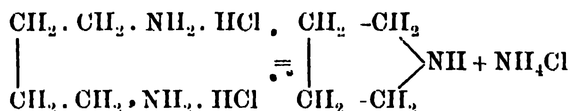
[1] *Annalen*, 1899, 305, 84.

giving off nitrogen, often with explosive violence. The longest unsaturated chain so far obtained is tetraphenyloctazene, and contains eight nitrogen atoms.[1]

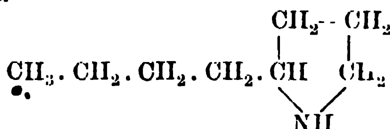


Only a very minute quantity was prepared, as it rapidly suffers decomposition.

Ring Formation. Ring formation seems to be governed by the same general principle which underlies that of the carbo-cyclic compounds, that is, the stability increases up to five and six-atom rings and is not seriously affected in such cases by the replacement of carbon by nitrogen at least to the extent of four atoms; in fact, unsaturated ring systems of five atoms appear to increase in stability with increase in the number of nitrogen atoms up to the above number. In considering the stability of ring structures containing one nitrogen atom it is interesting to follow the formation of the latter by the general method of heating the hydrochloride of the diamine, when ammonium chloride is removed and a saturated ring system produced. Tetramethylene-diamine hydrochloride, for example, gives pyrrolidine.



The same reaction takes place with pentamethylene-diamine, giving a six-atom ring; but the higher homologues give other products. The compound obtained by heating octomethylene-diamine and which was formerly supposed to yield a nine-atom ring has been shown to be butyl pyrrolidine.



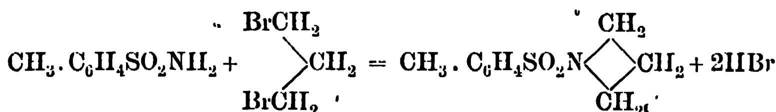
Although the four-ring system, trimethylene-imine, is produced by heating the hydrochloride of trimethylene-diamine, its formation is accompanied by a variety of complex by-products, whilst the corresponding ethylene-imine cannot be prepared by this method. Thus the five and six-ring systems appear to be the most stable.

Trimethylene-imine is probably produced by heating bromethylamine with potash, when hydrogen bromide is removed and a compound,

[1] Wohl and Schiff, *Ber.*, 1900, 33, 2745.

C_2H_5N, formed; nevertheless the substance behaves in many respects like an unsaturated compound, uniting with hydrogen chloride, giving chlorethylamine, and with sulphurous acid to form taurine. On the other hand, it may be argued that ethylene oxide shows the same tendency to pass into an open-chain structure by addition, so that at present no definite conclusion can be reached. Marckwald[1] is inclined to adopt the ring formula on the ground that the product of the action of benzenesulphonic chloride is insoluble in alkalis and consequently the original nitrogen was present as an imino group.

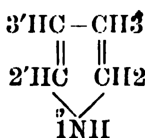
A trimethylene-imine ring can be prepared from trimethylene bromide and toluene sulphonamide.



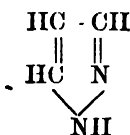
From this, the toluene sulphonyl group may be removed by reduction, leaving trimethylene-imine in the form of a liquid boiling at 63° with a strong ammoniacal smell. Like ethylene-imine it is very unstable and readily passes into an open chain by the action of acids.

Carbon-Nitrogen Ring Formation. The various types of reactions summarized in the foregoing paragraphs will explain the greater number of processes applied to the formation of heterocyclic ring systems, containing nitrogen. As the synthesis of six-atom rings containing one nitrogen atom will be discussed later under alkaloids, we shall illustrate the above reactions by reference to five atom rings containing from one to four atoms of nitrogen.[2] An attempt to extend the study to other ring systems would occupy more space than the theoretical value derived from such a comprehensive treatment of the subject would warrant.

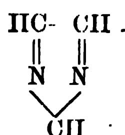
The system of nomenclature applied to these five-atom ring structures is to indicate the number and position of the nitrogen atoms in the first part of the name, to which the suffix *-ole* is then attached.



Pyrrole.



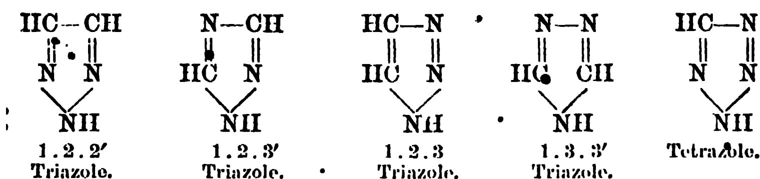
1.2 Diazole.



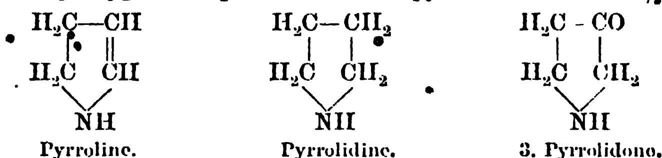
2.2′ Diazole.

[1] *Ber.*, 1899, 32, 2036.

[2] An account of 5-membered carbon-nitrogen rings is given by Ciamician. *Ber.*, 1904, 37, 4200.



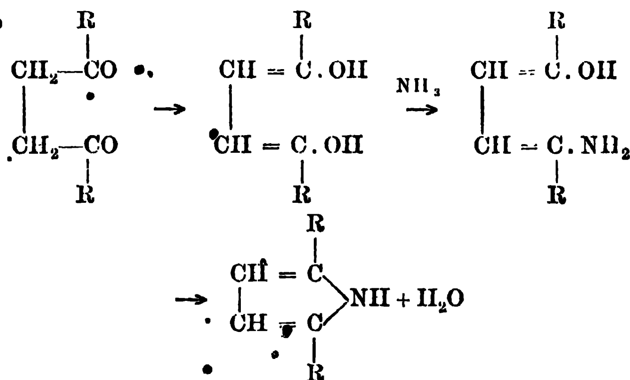
The various reduction products are indicated by adding the termination *-ine* to the name if two hydrogen atoms are added, and if four hydrogen atoms are introduced the termination *-idine* is added, whilst the presence of a ketone group in the ring is indicated by the suffix *-one*, &c. Thus pyrrole forms on reduction the compounds pyrroline and pyrrolidine, and if, in the last, two hydrogen atoms are replaced by oxygen, the product is called pyrrolidone.



The parent substances themselves exhibit for the most part weak basic characters, due no doubt to the acidic character of the unsaturated nucleus, for the basicity is immediately enhanced on reduction. Whereas pyrrole is weakly basic as well as weakly acidic (the hydrogen of the NH group is replaceable by alkali metals as in phenol), pyrroline has all the properties of a secondary base and pyrrolidine is still more strongly basic, with an ammoniacal smell resembling piperidine.

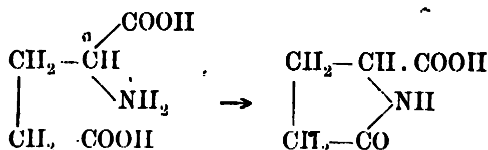
Among the methods used for obtaining members of the pyrrole series are :

1. The action of ammonia on 1.4 diketones which follows the course



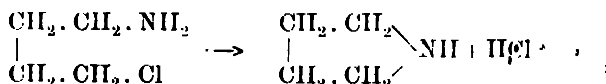
that is, the diketone isomerises to the tautomeric form.

2. The action of heat on glutamic acid,

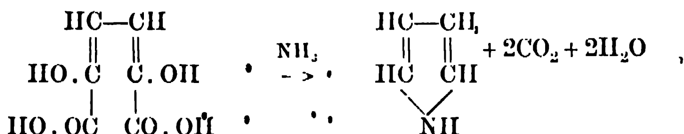


3. Succinimide, derived from succinic anhydride by the action of ammonia, may be regarded as a pyrrolidone, for it may be converted into pyrrolidine on reduction with sodium in alcoholic solution.

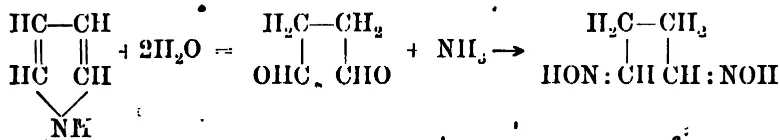
4. Pyrrolidine is also formed by heating the hydrochloride of tetramethylene diamine, or by removing hydrogen chloride from 5-chlorobutylamine.



5. Pyrrole itself is prepared by heating ammonium mucate, which is probably converted into the intermediate form, and then reacts with ammonia, at the same time losing carbon dioxide and water.[1]



It should be pointed out that the stability of the ring is greatly weakened by attaching oxygen to the carbon members of the ring. Succinimide, for example, is readily hydrolysed and the ring broken. But the non oxygenated derivatives are comparatively resistant to ring cleavage. It can, however, be effected if the open chain is prevented from closing by the presence of a reagent with which the compound can combine. Thus, the pyrrole ring can be broken by alkalis in presence of hydroxylamine. Water is taken up, ammonia expelled, and the dialdehyde, thus produced, unites with the reagent,

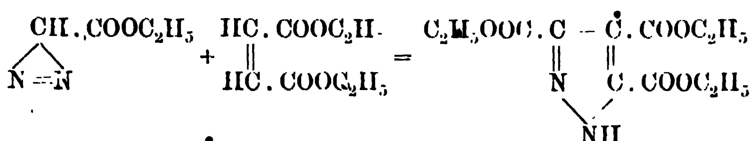


Pyrazole and its homologues have weak, but distinctly basic properties, forming salts and double salts and behaving as secondary bases.

[1] Ciamician, *Ber.*, 1904, 37, 4205.

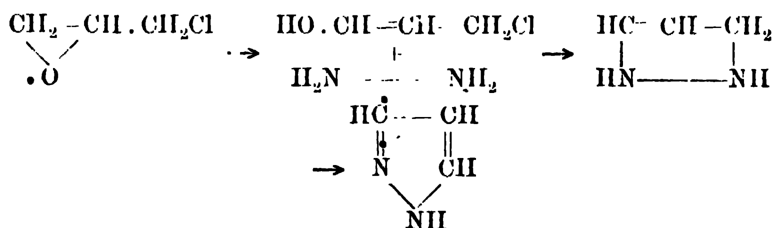
Its formation, and that of its numerous derivatives, may be accomplished by an extraordinary variety of synthetic methods.

1. A process of addition is illustrated by a method corresponding to the formation of pyrazole from acetylene and diazomethane already referred to (p. 204). Other acetylene and olefine derivatives may be substituted for acetylene, and diazoacetic ester for diazomethane. Fumaric ester unites with diazoacetic ester thus:

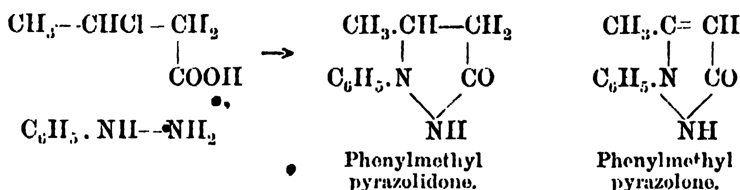


Where open-chain compounds combine by substitution, it is requisite that union takes place at two points. Combination, with simultaneous elimination of halogen acid and water or alcohol, is illustrated by the following:

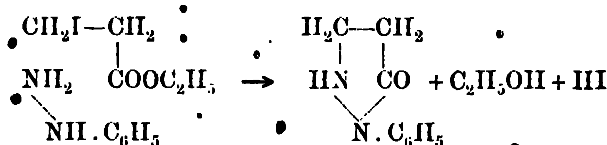
Epichlorhydrin and hydrazine combine in presence of zinc chloride, and at the same time hydrogen is eliminated and pyrazole is formed.



β-Chlorobutyric acid and phenylhydrazine give 2-phenyl, 3-methyl, 1-pyrazolidone, which, on oxidation, gives the corresponding pyrazolone:

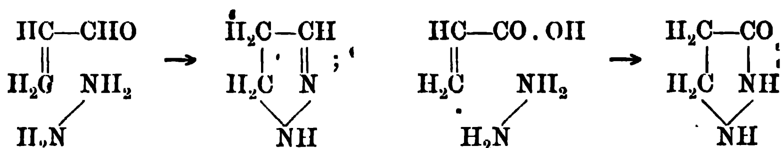


β-Iodopropionic ester and phenylhydrazine react in a similar way.

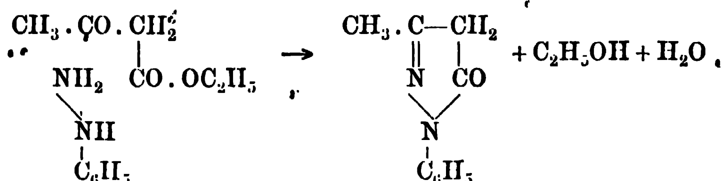


Substitution and intramolecular isomeric change occurring together

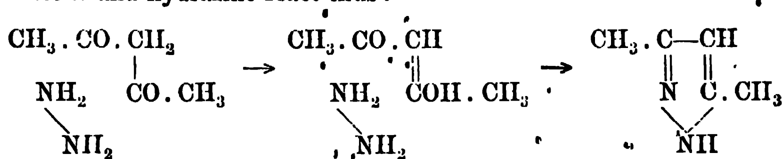
are illustrated by the union of acrolein and acrylic acid with hydrazine and its derivatives:



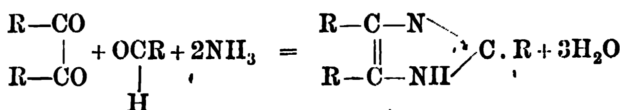
But the most prolific source of pyrazole compounds is that furnished by the method of Knorr, namely, the interaction of 1.3 diketones or ketonic esters with hydrazines. The most familiar example is that of acetoacetic ester and phenylhydrazine:



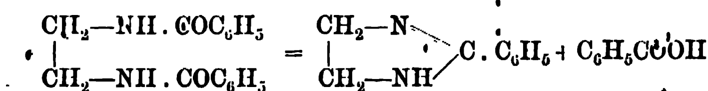
If a 1.3 diketone is used in place of a ketonic ester two molecules of water are removed and no oxygen appears in the product. Acetyl acetone and hydrazine react thus:



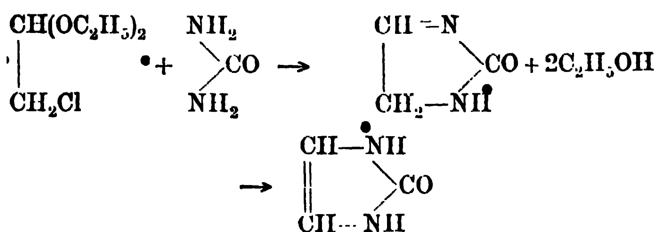
2.2′ diazoles (glyoxalines, iminazoles) are stronger bases than the foregoing and form stable salts with acids. The common method for obtaining them is by the combined action of ammonia or amine and aldehyde on an ortho diketone:



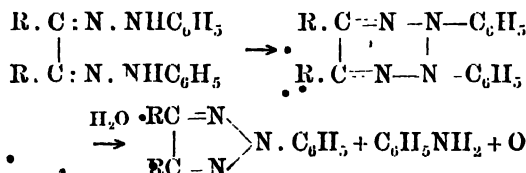
Another method is by the removal of a molecule of acid from a diacyl diamine:



Finally, the linking of a molecule of urea with chloracetal and removal of alcohol gives a diazolone.

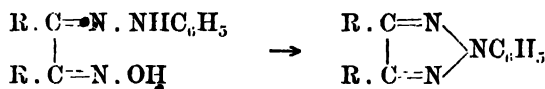


The 1.2.2′ triazoles (osotriazoles) are mostly oils with an alkaloidal smell, and weak basic characters. At the same time they are remarkably stable towards oxidising agents, the side-chains being oxidised like those of benzene derivatives to carboxyl. Nitro compounds and sulphonic acids can also be obtained by nitration and sulphonation in the ordinary way, whereas, in the case of pyrrole and pyrazole derivatives, special methods are requisite.[1] v. Pechmann was the first to prepare them by a reaction which illustrates the greater stability of the five carbon over that of the six-carbon ring. When an osazone is oxidised it is converted into a tetrazone, which, by the action of dilute mineral acids, loses one nitrogen group as primary amine.

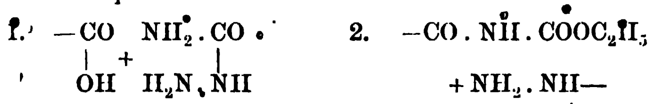


The free oxygen, which is liberated, acts upon and resinifies a portion of the material.

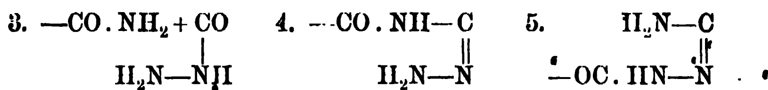
A second method consists in removing, by means of acetic anhydride or dilute alkali, the elements of water from the hydrazoxime of a 1.2 diketone,



The 1.2.3′ triazoles contain the atoms of the ring in the order —C—N—C—N—N— so that such combinations as the following might be anticipated:

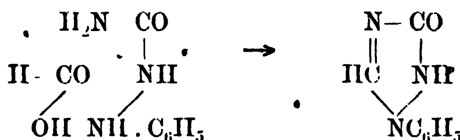


[1] *Indol- und Pyrrolgruppe*, by Angeli. Ahrens' *Vorträge*, 1912, 17, 312.

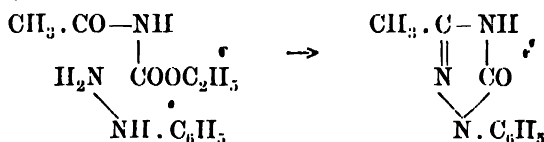


All these processes can be applied in one form or another, and one example will be given of each.

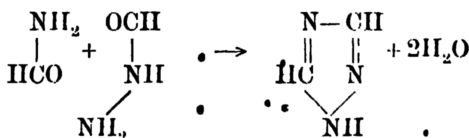
1. Formic acid combines with phenylsemicarbazide:



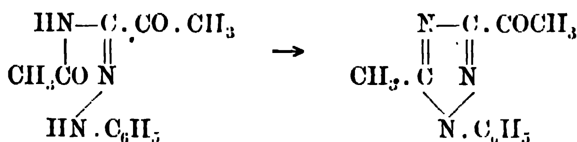
2. Phenylhydrazine reacts with acetylurethane:



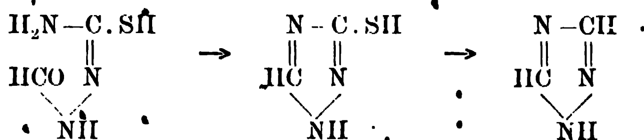
3. Formamide and formylhydrazide give triazole:



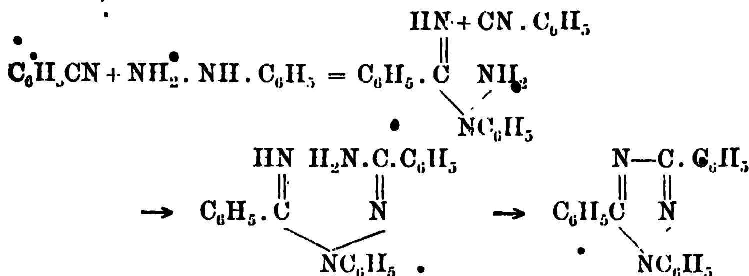
4. The fourth and fifth reactions are illustrated by intramolecular combination as follows:



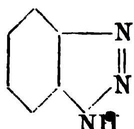
5. Formylthiosemicarbazide gives, on heating, mercaptotriazole, which, on oxidation with hydrogen peroxide, loses sulphur:



An interesting example of intermolecular isomeric change is that of the action of phenylcyanide on phenylhydrazine, which occurs in several phases:

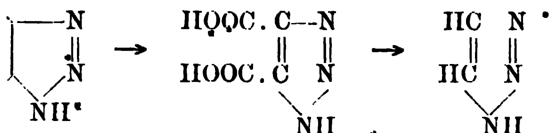


1 . 2 . 3 triazoles belong mainly to the aromatic series in the form of azimidobenzene and its derivatives:

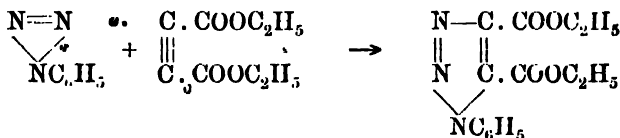


Azimidobenzene.

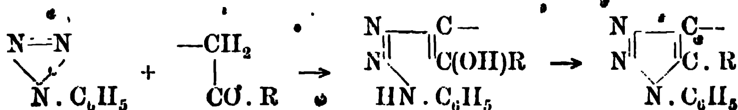
and few members of the single-ring system, obtained by direct synthesis, are known Like the foregoing, they are very stable, and may be obtained indirectly by oxidising and removing the benzene nucleus. Thus, azimidobenzene on oxidation gives the triazole dicarboxylic acid, from which carbon dioxide may be removed:



As azimidobenzene and its derivatives are readily prepared by a variety of methods, the formation of single-ring compounds affords no difficulty. The union of acetylene dicarboxylic ester with diazobenzolimide is an interesting modification of the pyrazole synthesis described on p. 204.

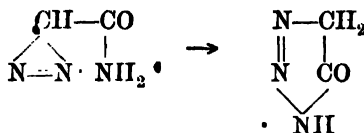


Diazobenzolimide also condenses with ketones, 1 . 3 diketones, and ketonic esters.[1]

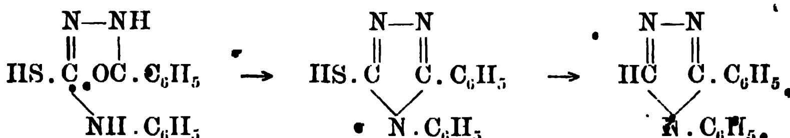


[1] Dimroth, *Ber.*, 1906, 39, 3920

Diazoacetamide, when warmed with alkali, is converted into triazolone:

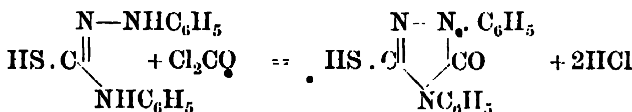


The 1.3.3′ triazoles, the fourth group of isomers, may be prepared from phenylthiosemicarbazide, $C_6H_5NH.CS.NH.NH_2$. On treatment with an acid chloride (benzoyl or acetyl chloride), the change occurs as follows:

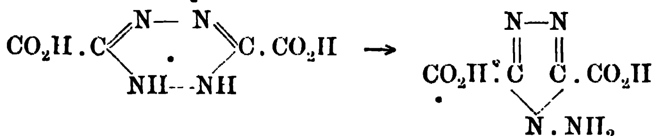


The sulphur can then be removed by oxidation.

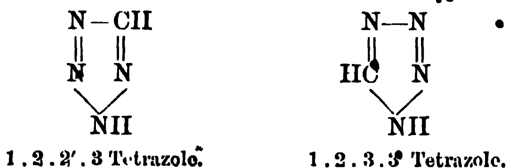
Diphenylthiosemicarbazide and carbonyl chloride can also be converted into a triazole derivative:



A reaction, which illustrates the greater stability of a five-atom compared with a six-atom ring, is the conversion of bis-diazoacetic acid by treatment with strong caustic potash into a triazole derivative:



Tetrazole should be represented by two isomeric compounds.



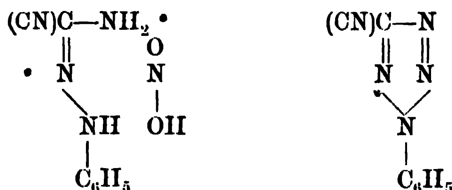
1.2.2′.3 Tetrazole. 1.2.3.3′ Tetrazole.

As a matter of experience, only one (the first of the above) is known. It is, in short, a case similar to that of methylpyrazole (Part II, p. 328), or of the single ortho compound in the benzene series.

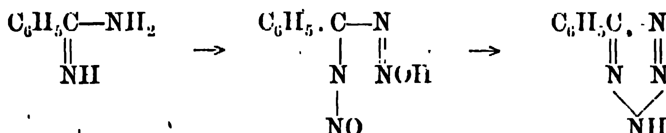
The tetrazoles are remarkably stable substances. Oxidation will destroy a side-chain, but leaves the tetrazole nucleus intact. Moreover, tetrazoles are characterised by acidic properties, in which the hydrogen of the NH group is replaceable by metals.

There are numerous methods by which the tetrazoles have been prepared, among which the following are included:

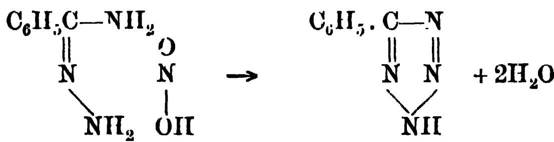
Bladin, who prepared cyanamidrazone by the action of cyanogen on phenylhydrazine, obtained the first tetrazole compound by acting on the former with nitrous acid:



Hydrolysis converts the cyanogen group into carboxyl, and oxidation has the same effect on the phenyl group. On splitting off carbon dioxide, tetrazole itself is formed as a solid, melting at 156°. Benzylidene amidine is converted by nitrous acid into the diazonitrosamine, which passes on reduction into 3-phenyl tetrazole:

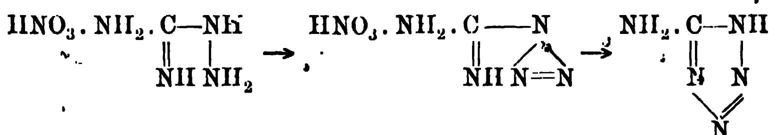


Hydrazides behave like the amidines with nitrous acid:



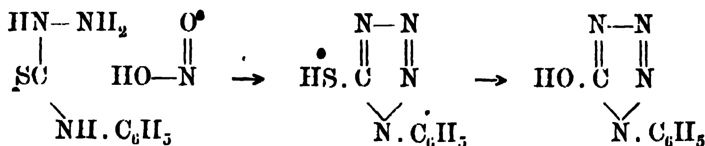
Aminoguanidine, inasmuch as it resembles a hydrazide, undergoes a similar change, and gives aminotetrazole.

The action of nitrous acid on the nitrate of the base gives a diazo-compound, which changes into the ring compound.[1]

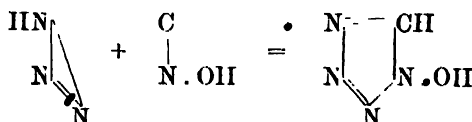


[1] Thiele, *Annalen*, 1892, 270, 1; Hantzsch and Vogt, *Annalen*, 1901, 314, 339.

In the same way phenylthiosemicarbazide may be used, and the sulphur subsequently removed by oxidation:



Hydroxytetrazole has been obtained by the action of sodium fulminate on azoimide.[1]



Six membered rings containing nitrogen are dealt with under *Alkaloids* (this volume, Part III).

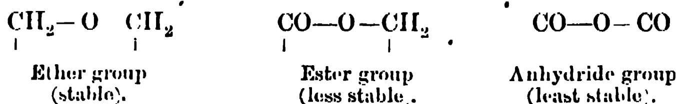
References.

Die heterocyklischen Verbindungen, by E. Wedekind. Veit, Leipzig, 1901.

The Organic Chemistry of Nitrogen, by N. V. Sidgwick. Clarendon Press, Oxford, 1910.

III. UNION OF CARBON AND OXYGEN

Carbon-Oxygen Chain Formation. Chain formation between carbon and oxygen, in which both atoms are saturated with hydrogen, is represented by the alcohols and ethers. In the latter only can the union be regarded as a stable one, and the stability is greatly diminished, as in the case of the carbon-nitrogen linkage, by replacing the hydrogen of the adjoining carbon by oxygen. The esters, and still more the anhydrides, thus formed, are easily hydrolysed.

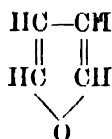


Union between oxygen and oxygen is even less stable than between nitrogen atoms, as seen in the peroxides and ozonides (p. 119), which decompose with explosive force. As only peroxides of acid radicals are known, it is impossible to say whether those with hydrocarbon radicals would exhibit greater stability.

Carbon-Oxygen Ring Formation. When we apply these principles to ring formation we find, as before, that they are not the only factors in determining the stability of the system, but that it is

[1] Palazzo and Marogna, *Chem. Soc. Abs.*, 1913, i. 300.

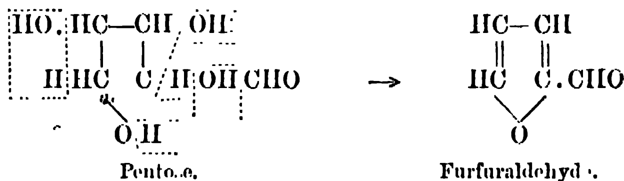
also largely influenced by the number of atoms composing the ring. Ethylene oxide is a low-boiling liquid, which was first obtained by removing hydrogen chloride by means of alkali from ethylene chlorhydrin; but it is extremely unstable, exhibiting in various ways a tendency to cleavage at the carbon-oxygen link, and to pass into an open-chain compound. The number of representatives of four-atom rings containing oxygen in the ring is very small. Trimethylene oxide has been prepared, and is a liquid boiling at 50°; but few of its derivatives are known. On the other hand, five-atom rings containing one atom of oxygen are comparatively stable, and comprise a very large number of compounds, termed furfurane derivatives. Though tetramethylene oxide, or tetrahydrofurfurane, has been prepared, the furfurane derivatives are for the most part unsaturated, furfurane, the parent substance, having the formula,



Furfurane.

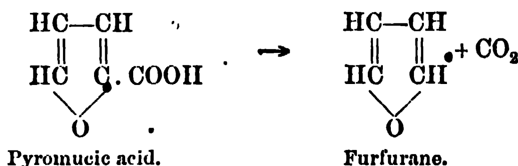
The scarcity of saturated ring compounds of this type would appear to indicate that they are not readily formed, and it is significant that among nitrogen ring compounds unsaturation has a distinct tendency in the direction of increasing the stability of the system.

There are various ways in which furfurane compounds are obtained. The oldest method is to distil carbohydrates with dilute sulphuric acid, which produces furfuraldehyde. The same compound is obtained by distilling a pentose with hydrochloric acid (Part III, p. 181).



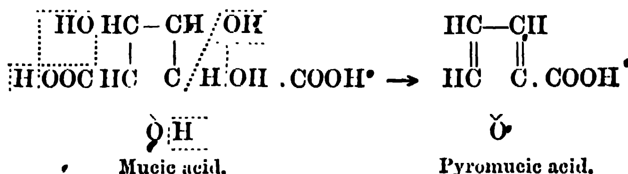
Pentose. Furfuraldehyde.

It is a colourless liquid with an empyreumatic smell, and boils at 162°. It has all the characteristic properties of an aromatic aldehyde, yielding an acid, pyromucic acid, on oxidation, and an alcohol, furfuryl alcohol, on reduction. The former, on distillation with lime or baryta, yields furfurane.



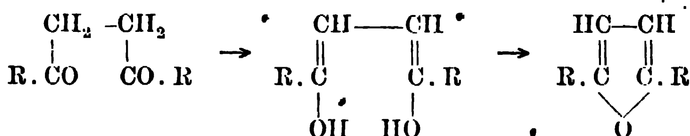
Pyromucic acid. Furfurane.

Pyromucic acid is also obtained, as its name implies, by distilling mucic acid (Part III, p. 29).

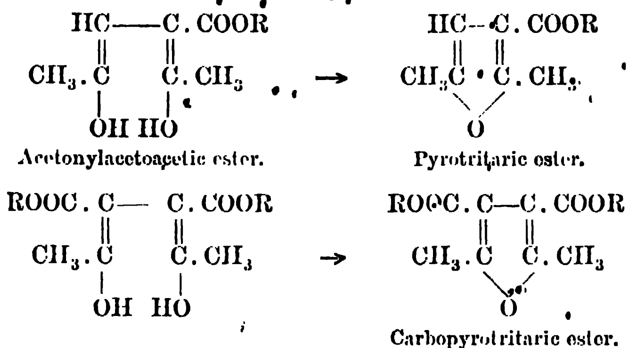


Mucic acid. Pyromucic acid.

Certain 1.4 diketones, which can react in the enol form, also give furfurane derivatives:



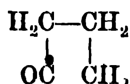
Thus, acetonylacetoacetic ester and diacetosuccinic ester give respectively the esters of pyrotritaric and carbopyrotritaric acids:

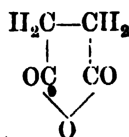


Acetonylacetoacetic ester. Pyrotritaric ester.

Carbopyrotritaric ester.

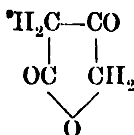
Among the derivatives of tetrahydrofurfurane containing oxygen in place of carbon may be included the lactones of γ-hydroxy acids and anhydrides of the succinic-acid series,


γ-Butyrolactone.

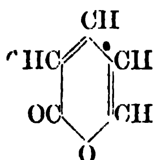

Succinic anhydride.

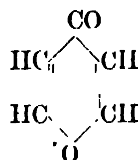
both of which are easily hydrolysed.

A compound isomeric with succinic anhydride is the lactone of γ-hydroxyacetoacetic acid or tetronic acid, which behaves in many ways like a 1.3 diketone.

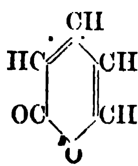

Tetronic acid.

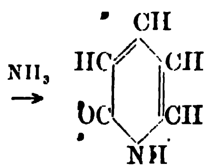
As in the five-atom ring systems, the commonest and most stable representatives of six-atom rings containing oxygen are unsaturated. Substances such as pentamethylene oxide, δ-valerolactone, and glutaric anhydride are known, but the number is small, and they are readily converted into open-chain compounds. On the other hand, those derived from α- and γ-pyrone are numerous and comparatively stable. As they are frequently met with among natural products, they possess a special interest:

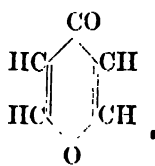

α-Pyrone.

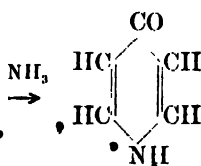

γ-Pyrone.

A further source of interest lies in the fact that by the action of ammonia they readily exchange the oxygen of the ring for NH, and thus pass into pyridones or derivatives of pyridine.


α-Pyrone.

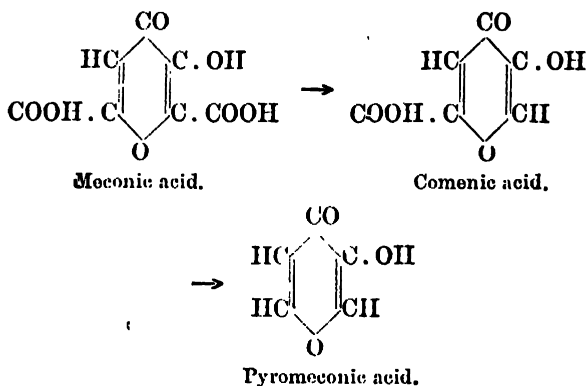

α-Pyridone.


γ-Pyrone.


γ-Pyridone.

Among the natural sources of the simpler pyrone compounds is

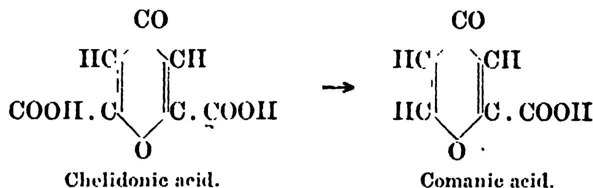
opium, which contains meconic acid, which on heating passes into comenic acid and pyromeconic acid:



Meconic acid. Comenic acid.

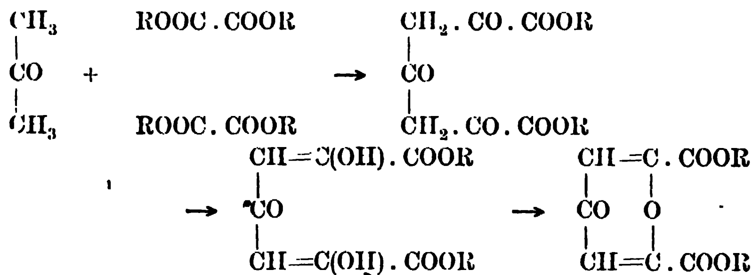
Pyromeconic acid.

Another natural source is the greater celandine (*chelidonium majus*), which contains an alkaloid combined with chelidonic acid or γ-pyrone dicarboxylic acid. On heating, it loses carbon dioxide and forms comanic acid:

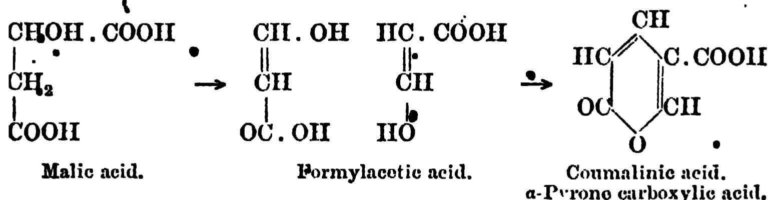


Chelidonic acid. Comanic acid.

Chelidonic acid has been prepared synthetically by condensing acetone with oxalic ester by means of sodium methoxide. The alcoholic solution yields, on boiling, chelidonic ester:

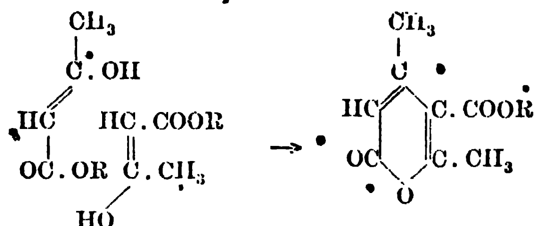


Coumalinic acid was obtained by v. Pechmann by warming malic acid with strong sulphuric acid, which removes water and carbon monoxide. Condensation may be represented as taking place by the union of the unstable intermediate product, formylacetic acid or its tautomeric form.

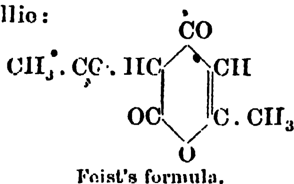


Malic acid. Formylacetic acid. Coumalinic acid. α-Pyrone carboxylic acid.

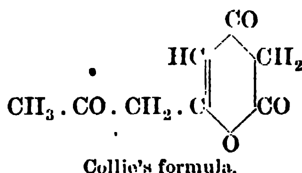
Dimethylcoumalinic acid (isodehydracetic acid) is another pyrone derivative, which is prepared by the action of sulphuric acid on acetoacetic ester and in other ways:



Dehydracetic acid was first obtained by Geuther from the residues from the preparation and distillation of acetoacetic ester, and is formed by heating acetoacetic ester alone or with acetic anhydride. Its structure has been the subject of much discussion, and the following alternative formulae have been proposed by Feist and Collie:

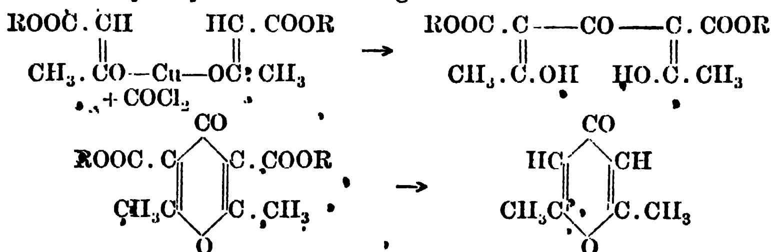


Feist's formula.



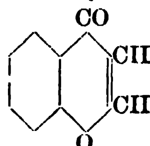
Collie's formula.

One of the most interesting of the pyrones is the dimethyl derivative obtained by heating dehydracetic acid under pressure and then dehydrating over sulphuric acid. It has also been prepared by the action of carbonyl chloride on the copper compound of acetoacetic ester and hydrolysis of the resulting ester:

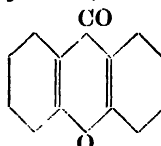


It forms well-defined salts with mineral acids, the latter combining with the cyclic oxygen atom, which acts as a quadrivalent atom.

Among the more complex of the pyrones are those in which the pyrone is fused with a benzene nucleus, in the form of benzo- and dibenzo-γ-pyrone compounds, which may be regarded as the parent



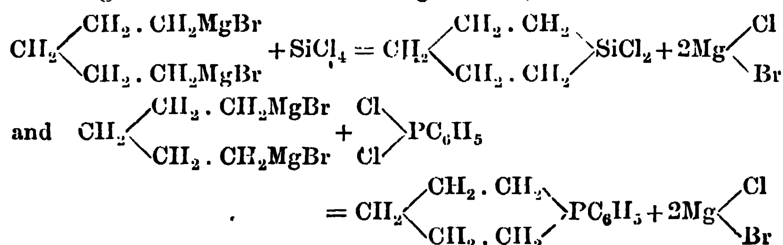
Benzopyrone
(coumarin).



Dibenzopyrone
(xanthone).

substances of a large and interesting variety of natural colouring matters belonging to the chrysin family, the structure of which has been determined in the majority of cases by synthesis. A study of these compounds is beyond the scope of the present chapter.

Cyclic compounds silicon, phosphorus, arsenic antimony, bismuth lead and tin forming one of the links in the ring have been obtained by Bygden [1] and by Grüttner and his collaborators.[2] The process consists in acting upon pentamethylene magnesium dibromide with the halogen derivative of the reacting element, thus:



$$CH_2\left<\begin{matrix}CH_2 \,.\, CH_2MgBr\\CH_2 \,.\, CH_2MgBr\end{matrix}\right. + SiCl_4 = CH_2\left<\begin{matrix}CH_2 \,.\, CH_2\\CH_2 \,.\, CH_2\end{matrix}\right>SiCl_2 + 2Mg\left<\begin{matrix}Cl\\Br\end{matrix}\right.$$

and

$$CH_2\left<\begin{matrix}CH_2 \,.\, CH_2MgBr\\CH_2 \,.\, CH_2MgBr\end{matrix}\right. + \begin{matrix}Cl\\Cl\end{matrix}\!>PC_6H_5$$

$$= CH_2\left<\begin{matrix}CH_2 \,.\, CH_2\\CH_2 \,.\, CH_2\end{matrix}\right>PC_6H_5 + 2Mg\left<\begin{matrix}Cl\\Br\end{matrix}\right.$$

REFERENCE.

Die heterocyklischen Verbindungen, by E. Wedekind. Veit, Leipzig, 1901.

[1] *Ber.*, 1915, 48, 1236.

[2] *Ber.*, 1915, 48, 1173; 1917, 50, 1549.

CHAPTER IV

DYNAMICS OF ORGANIC REACTIONS

Of the various means which have been employed to obtain information in regard to the mechanism of organic reactions, one of the most important is that afforded by a study of the velocity of change, and of the way in which this velocity is modified by variations in the conditions under which a given reaction occurs. In the early study of chemical dynamics, chief interest centred in the discovery of simple reactions, which, by reason of their freedom from any disturbing complications, might be made use of in testing the applicability of the law of mass action to account for the observed course of the change. Now, however, that the mass law, under given conditions with respect to temperature and the nature of the reaction medium, has been definitely established as the factor which determines the course of a given change, the main object of a dynamical investigation lies in the information which it affords in regard to the mechanism by which the final products of a reaction are produced from the original substances.

LAW OF MASS ACTION

Historical. That chemical change is not entirely determined by the operation of specific chemical affinities appears to have first been recognized by Wenzel[1] (1777), who, from his observations on the rate of solution of metals in acids, arrived at the conclusion that the rate of chemical action is proportional to the concentration of the substances entering into the reaction. A similar view was put forward by Berthollet in his *Essai de Statique Chimique* (1803). The fact that Berthollet's views, supported as they were by experimental evidence of a convincing kind, had but little influence on the trend of chemical theory at this period was doubtless due in large measure to the erroneous conclusion which he drew in regard to the influence of mass on the composition of chemical compounds. The proof that such composition is quite independent of the quantities of the reacting substances tended to

[1] *Lehre von der chemischen Verwandtschaft der Körper*, 1777.

bring the whole doctrine of mass action into disrepute, and for many years no further progress was made in the direction indicated by Berthollet's researches.

In the fifties Rose[1] and Malaguti[2] called attention to phenomena which undoubtedly indicated the important part played by the quantities of the reacting substances in chemical change, but no generalization of any importance was drawn by these observers. About the same time, Wilhelmy[3] studied the inversion of sucrose under the influence of acids, and arrived at the conclusion that the rate of transformation of the sucrose is at every moment proportional to its concentration. The agreement of the experimental data with the values, calculated from the equation which Wilhelmy deduced on the basis of the above proportionality, represents the first definite proof of the operation of mass in a chemical reaction according to a quantitative law (Part III, chap. 96).

Somewhat later, Berthelot and St. Gilles,[4] in a detailed study of the formation and decomposition of the esters, showed that the relative masses of the various substances involved determined the direction of the change. Whether change occurs in accordance with the upper or lower arrows in the formula



$$C_2H_5OH + CH_3.CO_2H \rightleftarrows CH_3.CO_2C_2H_5 + H_2O$$

depends, at a given temperature, on the relative quantities of the four substances concerned.

The part played by quantity or the mode of operation of mass in chemical change was first enunciated, however, in the form of a generalized statement by Guldberg and Waage[5] in 1867. If A and B represent two substances which are decomposed into A' and B', and it is assumed that under the same conditions A' and B' can react to form A and B, then, under the influence of the chemical affinities and the active masses of the reacting substances, a state of equilibrium will be reached which can be represented in the following manner. If the active masses of A, B, A' and B' be denoted by p, q, p' and q' respectively, and the affinity coefficients of the reactions $A + B \rightarrow A' + B'$ and $A' + B' \rightarrow A + B$ are represented by k and k', then in the condition of equilibrium $kpq = k'p'q'$ or $k/k' = p'q'/pq =$ constant. From experiments in which barium sulphate was treated with differently concentrated solutions of potassium carbonate, or

[1] *Ann. Physik*, 1855, 94, 481; 1855, 95, 96, 284, 426.
[2] *Ann. Chim. Phys.*, 1857 (3), 51, 328.
[3] *Ann. Physik*, 1850, 81, 413; Ostwald's *Klassiker*, No. 29.
[4] *Ann. Chim. Phys.*, 1862 (3), 65, 385; 1862 (3), 66, 5; 1863 (3), 68, 225.
[5] Ostwald's *Klassiker*, No. 104.

with solutions containing both potassium carbonate and sulphate, it was shown that the equilibrium condition in the reversible change $BaSO_4 + K_2CO_3 \rightleftarrows BaCO_3 + K_2SO_4$ is in agreement with the requirements of this theory. In the equilibrium state, the opposing reactions are exactly balanced, and the velocities of two opposed reactions are accordingly measured by kpq and $k'p'q'$ respectively. In other words, the rate of progress of a change in which several substances react together is determined by a specific constant and by the product of the active masses of the reacting substances.

In the further development of this idea, a certain amount of confusion arose in connection with the question whether the mass effect is solely dependent on the number of the reacting substances or on the number of the molecules of those substances which are involved in the actual molecular interchange. Kinetic considerations indicate that the latter view is the correct one, and thermodynamical reasoning leads to the same result.

Unimolecular Non-reversible Reactions. From the molecular kinetic standpoint, the simplest chemical changes are those in which the product or products of a reaction are directly formed as a result of the transformation of the individual molecules of the original substance. Such changes, which are not dependent on the interaction of two or more molecules, are solely determined by the law of probability. It is obvious that reactions which belong to this class are necessarily limited to certain types. Amongst them we find changes in which complex molecules are decomposed into simpler molecules and those in which intramolecular rearrangements are involved. Although no reaction may be said to be absolutely irreversible, those which belong to this group are characterized by the absence of any appreciable tendency on the part of the product or products of the reaction to react with the formation of the original substance.

From the fact that a unimolecular change is not dependent on the interaction of two or more molecules, and therefore of the approach of such molecules within the range of intermolecular influence, it is evident that the speed of a unimolecular change is entirely independent of the spacial distribution of the molecules, that is to say, of the volume occupied by a given quantity of the substance. Close packing of the molecules, which, in all cases where intermolecular actions are concerned, is conducive to increased speed of reaction, has no influence on the velocity of a unimolecular change.

If a represents the original quantity of a substance per unit of

volume, $(a-x)$ the quantity present after time t, then at this moment the velocity of the unimolecular change is given by

$$dx/dt = k_1(a-x) \quad (1)$$

which yields on integration

$$k_1 = \frac{1}{t} ln \frac{a}{a-x} \quad (2)$$

Throughout the course of the reaction, the expression on the right side of the equation (2) must remain constant, and k_1, which is the so-called velocity coefficient, is solely determined by the specific character of the reaction, provided that the temperature and the nature of the medium, in which the change occurs, are prescribed.

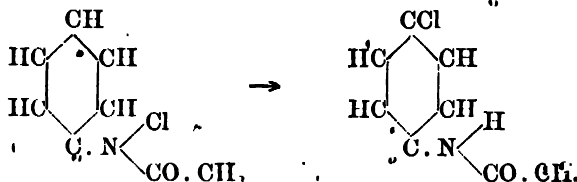
From equation (1) it is evident that the velocity coefficient represents the quantity of the original substance which would be transformed in unit time, if throughout this period of time the concentration were maintained constant and equal to unity.

If the integrated form of the equation is considered, it is further obvious that the time required for the transformation of a given fraction $(1/n)$ of the original substance is independent of the initial concentration, for $a/(a-x) = n/(n-1)$, and equation (1) may therefore be written in the form

$$t = \frac{1}{k_1} ln \frac{n}{n-1}$$

It is also clear that the value of the velocity coefficient of the unimolecular change is not in any way influenced by the particular unit in terms of which the concentration is expressed.

Velocity of Intramolecular Rearrangement in Halogen Acetanilides. This intramolecular change affords an example of a unimolecular non-reversible reaction. In presence of hydrogen chloride, acetylchloroanilide, for example, is gradually transformed into p-chloroacetanilide in accordance with the formula (Part II, p. 371)[1]



The rate of progress of the change can be readily followed by removing samples and adding them to excess of a potassium iodide

[1] J. J. Blanksma, *Rec. Trav. Chim. des Pays-Bas*, 1902, 21, 366; 1903, 22, 290.

solution and titration of the liberated iodine. This iodine corresponds with the undecomposed acetylchloroanilide present, for the *p*-chloroacetanilide is without action on the iodide. The following data were obtained in 20 % acetic acid solution at 25°.

t (*hours*)	*a*−*x* (*in c.c. of standard* $Na_2S_2O_3$ *solution*)	*k*
0	49.3	—
1	35.6	0.139
2	25.75	0.140
3	18.5	0.140
4	13.8	0.138
6	7.3	0.138
8	4.8	0.139

As the numbers in the third column indicate, the progress of the reaction can be satisfactorily accounted for on the assumption that the reaction is unimolecular, or of the first order.[1]

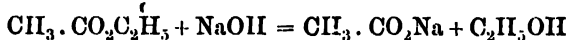
Polymolecular Non-reversible Reactions. In contrast with changes of the first order, the speed of a reaction, which involves the interaction of two or more molecules, increases as the volume containing a given quantity of the original substance or substances decreases. Such diminution in volume is accompanied by an increase in the frequency with which the molecules enter into collision or come within the range at which interaction between the several molecules becomes possible. This concentration effect, which becomes more pronounced as the order of the reaction increases, finds adequate expression in the equation which is obtained when the law of mass action is applied to a reaction of the second or higher order.

In the many reactions which belong to this group, the molecules actually involved in the change may be all identical, or in part so, or they may all be different. So far as the dynamical course of the reaction is concerned, the nature of the reacting molecules is, however, of no importance, the progress of the change during successive time intervals being solely determined by the number of the molecules involved in the actual process of molecular interchange.

Bimolecular Reactions. Changes belonging to the polymolecular non-reversible group are of the most varied nature, and include polymerisation phenomena, synthetic reactions, double decompositions, isomeric changes, &c. As a first example, we may consider the saponification of esters by the alkali hydroxides. In the case of

[1] In view of the observations of Orton it would appear that the intramolecular change of the chloroamine involves two stages and is therefore a composite reaction; cf. Orton and King, *Trans. Chem. Soc.*, 1911, **99**, 1369; also Orton and Jones, *Trans. Chem. Soc.*, 1909, **95**, 1456.

a simple ester (that is, the ester of a monobasic acid) the reaction is bimolecular, two molecules being involved, as indicated by the ordinary chemical equation



$$CH_3 . CO_2C_2H_5 + NaOH = CH_3 . CO_2Na + C_2H_5OH$$

The saponification proceeds at a rate which can be conveniently measured at temperatures between 0° and 25° if dilute solutions are employed. If the original solution contains a grm.-mols. (mols) of ester and b mols of hydroxide per unit volume, and if x mols of ester have been saponified after time t, the concentrations of the reacting substances at this moment will be $a-x$ and $b-x$ respectively. According to the mass law, the speed of the change will be given by

$$dx/dt = k_2 (a-x)(b-x)$$

and this on integration becomes

$$k_2 = \frac{1}{(a-b)t} \ln \frac{b(a-x)}{a(b-x)}.$$

In the following table are given the data obtained by Reicher[1] for the saponification of ethyl acetate at 15·8°, the alkali being present in excess ($b>a$) in the one experiment, whilst the ester predominated in the second ($a>b$). The quantities of saponified ester (x) are expressed in terms of the standard acid solution which was used in following the progress of the change.

Excess of alkali hydroxide.			*Excess of ester.*		
t (*minutes*)	x	k_2	t (*minutes*)	x	k_2
0	0	—	0	0	—
3.74	7·76	3·17	2·57	8·23	3·45
6.29	11·49	3·48	5·03	13·39	3·46
10.48	15·81	3·43	7·35	17·97	3·45
13·60	18·22	3·41	9·57	20.93	3·41
∞	29.03	—	∞	21·12	—

If the reacting substances are present in equivalent proportions ($a = b$), the rate of change at time t is given by

$$dx/dt = k_2 (a-x)^2$$

from which

$$k_2 = \frac{1}{t} \frac{x}{a(a-x)}.$$

That this is in agreement with the actual course of saponification under these conditions is shown by the following data for an experiment at 24·7° with a solution in which the concentrations of both ester and alkali hydroxide were 0·025 mol per litre.[2]

[1] *Annalen*, 1885, **228**, 257; 1886, **232**, 103; 1887, **238**, 276.
[2] Arrhenius, *Zeit. phys. Chem.*, 1887, **1**, 110.

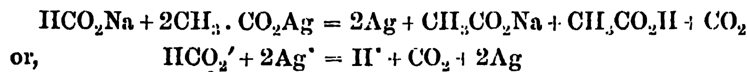
t (*minutes*)	$a-x$ (*in c.c. of standard acid*)	k_2
0	8.04	—
4	5.30	0.0159
6	4.58	0.0157
8	3.91	0.0161
10	3.51	0.0160
12	3.12	0.0163
15	2.74	0.0160
20	2.22	0.0163

Saponification experiments with different bases have shown that the reaction only proceeds in accordance with the above equations in the case of the strong bases, that is to say, those which are almost completely ionised in dilute solution. With weak bases the rate of saponification falls off very much more quickly than would be anticipated on the assumption that the velocity is at every moment proportional to the product of the concentrations of the ester and the base. If, however, we assume that the active mass of the base is represented by that portion which is ionised, in other words, that saponification is due to the hydroxyl ion, the differences in the behaviour of strong and weak bases can be accounted for quite readily. From these observations it is necessary to conclude that the saponification of an ester should be represented by the equation



$$CH_3.CO_2C_2H_5 + OH' = CH_3.CO_2' + C_2H_5OH$$

Termolecular Non-reversible Reactions. According to Noyes and Cottle,[1] the reduction of silver acetate by sodium formate in dilute aqueous solution affords an instance of an organic reaction in which three molecules are involved in the intermolecular transaction which gives rise to the products of the change. The order of the reaction is therefore in agreement with what would be anticipated on the basis of the ordinary chemical equation,



$$HCO_2Na + 2CH_3.CO_2Ag = 2Ag + CH_3CO_2Na + CH_3CO_2H + CO_2$$

or, $$HCO_2' + 2Ag^{\cdot} = H^{\cdot} + CO_2 + 2Ag$$

In the investigation of the progress of this reduction process, experiments were made at 100°, samples of the reaction mixture being forced over from the steam-jacketed tube into an ice-cold solution of potassium thiocyanate. By this means the reaction was brought to a standstill and the unchanged silver salt reacted with an equivalent quantity of the thiocyanate.

Denoting the initial equivalent concentrations of the formate and acetate by a and b, then, if the reaction is of the third order, the rate of

[1] *Zeit. physik. Chem.*, 1898, 27, 579.

change when the original concentration has diminished by x will be given by

$$dx/dt = k_3(a-x)(b-x)(b-x),$$

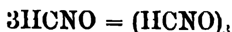
and this can be integrated and the termolecular velocity coefficient, k_3 evaluated in terms of a, b, x, and t.

The following data were obtained in an experiment in which the initial a and b values were each equal to 0·05. For comparative purposes the values of the bimolecular velocity coefficient k_2 are also given in the fourth column :–

t (*minutes*)	x	k_3	k_2
0	0	—	—
3	0·00967	35·8	1·60
8	0·01811	37·6	1·46
16	0·02532	38·8	1·28
25	0·02952	37·6	1·16
45	0·03371	37·4	0·92
80	0·03950	37·5	0·75

Comparison of the numbers under k_3 and k_2 shows that the former series is practically constant, whereas those of the latter series fall continuously as the reaction proceeds. In other experiments with different initial concentrations, the new values obtained for the termolecular velocity coefficient are approximately the same as in the example given above, and from this the authors conclude that the reaction in question is really termolecular.

The number of such termolecular reactions is very limited, but a further example has been found by van 't Hoff in the polymerisation of cyanic acid, the mechanism of which is therefore in accordance with the equation ordinarily employed to represent the polymerisation process, namely,



$$3HCNO = (HCNO)_3$$

In general, reactions of a higher order are quite exceptional. In the bromination of benzene, in presence of iodine as catalyst, Bruner claims to have found an example of a quadrimolecular reaction, and, if his conclusion is accepted, this reaction probably represents, from the point of view of the intermolecular transaction which is involved, the most complicated instance of a non-reversible organic change which has been dynamically investigated up to the present.

Determination of the Order of a Reaction. Since the expressions for the velocity coefficients of reactions of the first, second, third, &c., order are quite different in form, it is evident that dynamical data may be utilised in drawing conclusions relating to the mechanism of any given change. In the following discussion of the methods which may be employed in such investigations, it will be

assumed that the reactions in question are of the non-reversible type and that the final products are directly formed from the initial reacting substances.

Velocity Coefficient Method. The most obvious method of procedure consists in the utilization of the dynamical data to calculate the uni-, bi-, ter-, and quadri-molecular velocity coefficients. According to whether k_1, k_2, k_3, or k_4 remains constant, the conclusion might be drawn that the reaction is of the first, second, third, or fourth order. Although the application of this method has led to results which, in a large number of cases, leave no room for doubt as to their validity, experience has shown that erroneous deductions may not infrequently be made from the observed constancy of one or other of the expressions for the velocity coefficients. If, as the reaction proceeds, disturbances arise in consequence of the action of one of the final products on one or other of the original substances, it is evident that the data representing the progress of the reaction may indicate the constancy of a velocity coefficient which does not correspond with the real order of the reaction. On this account, measurements relating to the initial stages of the reaction will in general furnish a more satisfactory basis for the deduction of the order of the change.

Initial Velocity Method. This method, first employed by van 't Hoff,[1] involves the determination of the speed in the early stages of the reaction and of its dependence on the concentration of the original substance or substances. If the reacting substances are present in equivalent proportions, the average speed v_1 during the initial stage of the reaction will be given by

$$v_1 = -\frac{\Delta C_1}{\Delta t_1} = k C_1^n, \qquad (1)$$

where C_1 is the average concentration of the reacting substances during the time interval Δt_1 and n is the order of the reaction. If C_2 is the average concentration during a similar time interval Δt_2 in a second experiment, then

$$v_2 = -\frac{\Delta C_2}{\Delta t_2} = k C_2^n. \qquad (2)$$

From (1) and (2)

$$v_1/v_2 = \left(\frac{C_1}{C_2}\right)^n,$$

or

$$n = \frac{\log v_1 - \log v_2}{\log C_1 - \log C_2}.$$

[1] *Studies in Chemical Dynamics*, by J. H. van 't Hoff, trans. by T. Ewan. Williams & Norgate (1896).

In carrying out experiments to determine n in this way, the concentrations C_1 and C_2 should not be too nearly equal, and the time intervals should be chosen so as to allow of the accurate estimation of the average speed during this period. The magnitude of the initial period will be determined by the accuracy with which the progress of the reaction can be followed, but as a general rule it will be convenient to choose the time intervals in such a way that from 10–20 per cent. of the reacting substances have disappeared. In practice, this method is particularly useful in cases where the final products give rise to disturbing secondary reactions, for such products will obviously have least influence when the quantities formed are relatively small.

Method of Equifractional Parts. This method, which was first suggested by Ostwald,[1] consists in comparing the times which are required for the decomposition of the same fractional amount of the reacting substances, when the initial concentration is varied. If we compare the influence of the concentration on the time required for the disappearance of a definite fraction $(1/n)$ of the original reaction mixture, by reference to the expressions for the velocity coefficients of reactions of the first, second, and third order with equivalent concentrations of the reacting substances, it is seen that this influence is quite different in the several cases:

Unimolecular reaction. $t = \frac{1}{k_1} ln \frac{a}{a - a/n}$, that is, t is independent of a.

Bimolecular reaction. $t = \frac{1}{k_2} \frac{a/n}{a(a - a/n)}$, that is, t varies inversely as a.

Termolecular reaction. $t = \frac{1}{k_3} \frac{a/n(2a - a/n)}{2a^2(a - a/n)^2}$, that is, t varies inversely as a^2.

From the above relationships it is evident that experiments, in which the concentration of the reaction mixture is varied, afford a simple means of determining the mechanism of the irreversible change. Disturbances from side reactions (see later) are to a large extent eliminated by this method of procedure, and only influence the result obtained, in so far as the relative importance of the side-reactions varies with the concentration of the reacting substances. By comparison of the time intervals required for the disappearance of successive equifractional amounts of the original substances in parallel experiments with different initial concentrations, an estimate

[1] *Zeit. physik. Chem.*, 1888, 2, 127.

may be formed of the extent to which the principal reaction is disturbed by subsidiary reactions in its different stages.

Isolation Method. As its name implies, this method consists in arranging the conditions of the dynamic experiments so that one of the reacting substances is isolated from the rest in so far as its influence on the course of the reaction is concerned. This can be effected quite readily, for the condition of isolation is attained if the concentrations of the reacting substances are so arranged that the active masses of all but one remain sensibly constant during the whole process.

If A and B react in accordance with the equation



$$mA + nB \longrightarrow pC + qD + \ldots$$

and B is present in relatively large amount, then according to the law of mass action

$$-\frac{dC_A}{dt} = kC_A^m \cdot C_B^n;$$

but since C_B is practically constant, the rate of change may be written

$$-\frac{dC_A}{dt} = k' C_A^m,$$

and according to this equation the course of the reaction will be determined by the number (m) of molecules of the isolated substance A which are involved in the actual process of molecular interchange, although $m + n$ molecules are in reality involved. In a similar manner, the value of n may be determined in a separate series of experiments in which the substance B is isolated. In the case of more complicated reactions, this method is of great utility, and has been frequently applied in the systematic investigation of organic reactions.

By application of one or more of the above methods, it is possible to obtain information in regard to the part played by each of the several substances which take part in a chemical change. Although in the discussion of these methods it has been presumed that the reactions are simple and irreversible, the application is by no means limited to reactions of this type. Under suitable conditions the methods may also be applied to the more complex changes in which simultaneous or consecutive reactions are involved.

In the following pages examples will be given of reactions which have been investigated in this manner.

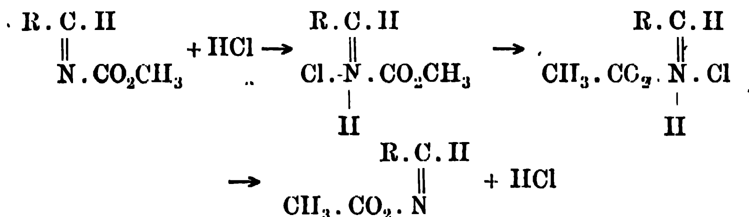
Stereo-chemical Changes. In view of the simple character of the isomeric transformation, the dynamical course of stereo-chemical

changes is of particular interest. The investigation of the rate of conversion of syn-aldoxime acetates into the corresponding anti-forms by Ley,[1] has shown that the reaction proceeds in accordance with the unimolecular equation.

The change occurs in absolute alcoholic solution in presence of hydrogen chloride as catalyst, and can be followed by the addition of removed samples of the solution to an ice-cold aqueous solution of sodium acetate, the mixture being then heated for some time at 80°, when the unchanged syn-aldoxime acetate is converted into the corresponding nitrite with the liberation of acetic acid, which is titrated with standard alkali. The following data were obtained in an experiment with anis-syn-aldoxime acetate at 25° in presence of 0·01 normal HCl as catalyst.

t (*minutes*)	$a-x$	$k_1 = \frac{1}{t} \log \frac{a}{a-x}$
0	0·0100	—
10	0·00551	0·0256
20	0·00318	0·0248
30	0·00199	0·0239
40	0·00118	0·0255

In regard to the catalytic action of the acid, it may be supposed that an intermediate additive compound is formed, and that this undergoes stereo-isomeric change, the acid being subsequently liberated from the isomeric form as represented by the formula



In this connection, reference may be made to the remarks on catalytic reactions on p. 326.

Conversion of Diazoamino- into Aminoazo-compounds. The transformation of diazoaminobenzene into aminoazobenzene, which takes place when aniline hydrochloride or other aniline salt is added to an aniline solution of the diazoamino-compound, affords a further instance of an intramolecular change which has been investigated dynamically. The speed can be measured conveniently at 25°- 50°, samples of the reaction mixture being run into caustic soda solution in order to stop the reaction, and the unchanged diazoamino-compound

[1] *Zeit. physik. Chem.*, 1895, 18, 376.

estimated by boiling with dilute acid and collecting the nitrogen which is liberated by its decomposition.

The experimental data obtained by Goldschmidt and Reinders[1] show that the reaction progresses in accordance with the equation for a unimolecular change. For a given concentration of the diazo-amino-compound, the velocity coefficient is proportional to the concentration of the aniline hydrochloride. On the other hand, when the concentration of the aniline salt is fixed, experiments with different concentrations of the diazoamino-compound lead to practically the same value of the velocity coefficient.

These observations indicate that the aniline hydrochloride plays the part of a catalyst in the transformation of the diazoamino-compound.

When other aniline salts, e. g. the trichloracetate and dichloracetate, are substituted for the hydrochloride, the nature of the reaction is unchanged, but the velocity coefficients show appreciable differences.

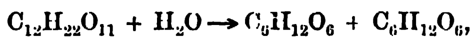
For solutions containing 0·5 mol diazoaminobenzene and 0·1 mol aniline salt per litre, the velocity coefficients at 25° were found to be 0·0060, 0·00437, and 0·00205 for the chloride, trichloracetate, and dichloracetate respectively.[2] Since the speed of the reaction diminishes with the strength of the acid, it is supposed that the catalytically active components are not really the aniline salts, but the free acids which result from their dissociation.

Apropos of this reaction, reference may be made to the fact that aminoazobenzene is formed when diazoaminobenzenetoluene is dissolved in aniline in presence of an aniline salt. Dynamic measurements show that the speed of this reaction is identical with that observed in the transformation of diazoaminobenzene, and it therefore seems probable that the diazoaminobenzenetoluene is primarily transformed into diazoaminobenzene in accordance with the equation



$$C_6H_5N:N.NHC_6H_4.CH_3 + C_6H_5NH_2 = C_6H_5.N:N.NHC_6H_5 + CH_3.C_6H_4.NH_2$$

Hydrolysis of Sucrose and Esters. As already mentioned, the study of the inversion of aqueous solutions of sucrose in presence of acids afforded the first proof that reaction velocity is at every moment proportional to the concentration of the decomposing substance. In accordance with the equation



$$C_{12}H_{22}O_{11} + H_2O \rightarrow C_6H_{12}O_6 + C_6H_{12}O_6,$$

the reaction is bimolecular and its rate of progress is found to be in

[1] *Ber.*, 1896, 29, 1369. [2] *Ber.*, 1896, 29, 1899.

agreement with the dynamic equation for a bimolecular change. Since in sucrose solutions, which are not too concentrated, the water is present in considerable excess, its active mass remains practically constant, and it is therefore not surprising to find that the values obtained for the unimolecular velocity coefficient k_1 exhibit much the same degree of constancy as the values of the bimolecular coefficient k_2 (Part III, p. 96).

If a and b are the concentrations of the sucrose and water respectively, then $k_2 = \frac{1}{(a-b)t} \ln \frac{a(b-x)}{b(a-x)}$, and since x is at all times very small in comparison with b, the equation may obviously be written in the same form as the equation for a true unimolecular change, viz.

$$k_1 = \frac{1}{t} \ln \frac{a}{a-x}$$

The speed of the sucrose inversion may be readily followed by observations of the rotation of a beam of plane polarised light, and if α_0, α_t and $-\alpha_\infty$ denote the rotations at the commencement, after time t and when the rotation has reached its final value, it is obvious that $\alpha_0 + \alpha_\infty$ affords a measure of a, and $\alpha_t + \alpha_\infty$ a similar measure of $a - x$.

The following table contains the data for the inversion of a 20 per cent. solution of sucrose at 25° under the influence of 0·5 normal lactic acid. For this solution the values of a and b may be taken as 0·628 and 45·3 respectively. The observed rotations after measured time intervals are shown in the second column; the numbers in the third and fourth give the values of $a-x$ and $b-x$, and columns 5 and 6 show that the uni- and bi-molecular velocity coefficients remain satisfactorily constant. The inversion of cane sugar by an acid in aqueous solution affords therefore an instance of a bimolecular change, the course of which is represented quite satisfactorily by the equation for a unimolecular reaction.[1]

t (*minutes*)	α	$a-x$	$b-x$	$k_1 . 10^4$	$k_2 . 10$
0	+34·50°	0·628	45·3	—	—
1435	31·10°	0·581	45·3	0·235	0·525
4315	25·00°	0·496	45·2	0·236	0·526
7070	20·16°	0·429	45·1	0·234	0·517
11360	13·98°	0·313	45·0	0·231	0·511
14170	10·61°	0·297	45·0	0·230	0·509
16940	7·57°	0·254	44·9	0·232	0·514
19820	5·08°	0·220	44·9	0·229	0·510
29930	−1·65°	0·126	44·8	0·233	0·518
α_∞	−10·77°	0	44·7	—	—

[1] Although the inversion of sucrose and similar changes are often quoted as examples of reactions of the first order, it seems to the author that this is a misnomer, for the apparent unimolecular character of these changes is entirely determined by the particular concentration relationships obtaining under the usual conditions in which the reactions are carried out.

The polarimetric method employed in following the progress of sucrose hydrolysis affords an example of the application of physical methods in determining the quantities of substances in solution. Although such methods may in certain cases afford accurate results, it seems likely that the accuracy attainable in the polarimetric method of determining the speed of the inversion of sucrose has been exaggerated. Not only has the hydrolysing acid an influence on the rotatory powers of the different sugars involved in the chemical change, but the fact that glucose and laevulose undergo mutarotation will also have an influence on the observed rotation. Under these circumstances it seems improbable that the polarimetric data afford a measure of the rate of change, which is as reliable as that attainable in the case where chemical methods of estimation are employed.

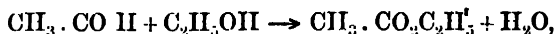
It has been supposed that the hydrolysis of sucrose by dilute acids deviates from the requirements of the mass law as expressed by the uni- or bi-molecular equation and that in the early stages of the reaction the velocity is practically constant.[1] This linear period is undoubtedly characteristic of the hydrolytic change when brought about by small quantities of enzymes. Recent experiments[2] indicate, however, that the analogy between acid and enzyme hydrolysis, which would be indicated by such a parallelism, has no foundation in fact, and that, within the limits of experimental error, the rate of sucrose hydrolysis, both under the influence of very dilute and more concentrated acids, is at all stages determined by the concentration of non-hydrolysed substances.

The process of ester hydrolysis in dilute aqueous solution under the catalytic influence of acids is in many respects similar to sugar inversion from the dynamic point of view. Although it has been shown recently[3] that the hydrolysis of methyl acetate in presence of hydrochloric acid does not proceed to completion, but that an equilibrium condition is reached when about 95 per cent. of the ester has been hydrolysed, yet for practical purposes the reaction may be regarded as non-reversible. The data representing the progress of the change are found to give a satisfactorily constant value for the unimolecular velocity coefficient, a circumstance which is due to the relatively large active mass of the water, for, in reality, the process of ester hydrolysis is a bimolecular change.

[1] Armstrong and Caldwell, *Proc. Roy. Soc.*, 1904, A, 74.
[2] Worley, *Proc. Roy. Soc.*, 1912, A, 87, 555; cf. also Rosanoff, Clark, and Sibley, *Journ. Amer. Chem. Soc.*, 1911, 33, 1911.
[3] Worley, *Proc. Roy. Soc.*, 1912, A 87, 582.

Both the above reactions have been largely used as a means of measuring the relative affinities of acids, for in dilute acid solutions the speed of both is very nearly proportional to the hydrogen ion concentration. The relative affinity values, obtained in this way, are parallel with the affinity coefficients obtained by electrical conductivity measurements, and, on this account, the two reactions have played an important part in connection with the development of the hydrogen ion theory of acids.

Esterification in Alcoholic Solution. In many respects this reaction resembles the two which have just been discussed, for according to the equation



$$CH_3 . CO_2H + C_2H_5OH \longrightarrow CH_3 . CO_2C_2H_5 + H_2O,$$

we have to deal with a bimolecular change, which, in consequence of the large excess of alcohol, may be expected to take place in accordance with the unimolecular formula. In presence of an acid catalyst this is actually the case, as may be seen from the data in the following table for the esterification of acetic acid in presence of hydrochloric acid.[1] In the parallel experiment are given the data obtained in the esterification of phenyl acetic acid in presence of picric acid as catalyst.[2]

Acetic acid 0·1 *mol*, HCl 0·025 *mol per litre.* *Temperature* 11·5°.			*Phenylacetic acid* 0·2372 *mol per litre.* *Temperature* 25°.		
t (*hours*)	$a - x$ (*in c.c. alkali*)	k_1	t (*hours*)	$a - x$ (*in c.c. alkali*)	k_1
0	60·4	-	0	11·86	—
1	55·1	0·0399	2·3	10·73	0·0187
2	50·3	0·0397	16·3	6·37	0·0166
3	45·9	0·0397	21·9	5·39	0·0156
4	41·9	0·0397	42·1	2·70	0·0152
5	38·2	0·0398	65·0	1·31	0·0147
6	31·9	0·0397			

Although the numbers under k_1 are quite constant in the acetic acid experiment, there is a marked diminution in the successive values of k_1 in the case of the phenylacetic acid. The difference is no doubt connected with the fact that small quantities of water, when added to water-free alcohol, reduce the velocity of esterification to a very large extent.[3] Since water is formed by the esterification of the acid, it may be expected that this will have a retarding influence on the progress of the change if the alcohol employed as solvent is nearly anhydrous. If, on the other hand, water is present in the alcohol in larger proportion, that which is formed during the

[1] Sudborough and Lloyd, *Trans. Chem. Soc.*, 1899, 75, 467.
[2] Goldschmidt and Wachs, *Ber.*, 1896, 29, 2208.
[3] Goldschmidt. *Ber.*, 1895, 28, 3218; 1896, 29, 2208. Goldschmidt and Sunde, *Ber.*, 1906, 39, 711. Goldschmidt and Udby, *Zeit. physik. Chem.*, 1907, 60, 728.

reaction will have comparatively little influence on the progress of the reaction. It seems probable, therefore, that the difference between the two results is due to the difference in water content of the alcohol used in the esterification, a satisfactory constant being obtained only when the alcohol is not too 'dry'.

The retarding influence of water on the esterification process is by no means characteristic of this reaction, for the velocities of many other acid-catalysed reactions are also depressed to a very large extent on the addition of very small quantities of water.[1] It is probable that the phenomenon is due to a change in the catalyst, the acid being very much more active in alcoholic solution than it is in aqueous solution. Since dilute aqueous and alcoholic solutions of the mineral acids are both ionised to about the same extent, according to conductivity measurements, it follows that the ordinary acid ions which are responsible for the transport of the electric current through the solutions cannot be regarded as the agents responsible for the catalytic activity. Various considerations indicate that the electrolytic hydrogen ions, present in aqueous solutions of acids, are hydrated, and it is therefore possible that the catalytically active ions are the simple unhydrated hydrogen ions. In the aqueous solution of a mineral acid, the proportion of such simple ions must be much smaller than in a corresponding alcoholic solution, the difference in concentration being determined by the difference in the affinity of the simple hydrogen ions for water on the one hand, as compared with their affinity for alcohol on the other.[2]

In the absence of a catalysing acid, the esterification of an acid in alcoholic solution proceeds otherwise. Whereas the experimental data yield decreasing values for the unimolecular velocity coefficient, fairly constant numbers are obtained when the bimolecular coefficient is calculated. According to Goldschmidt, this is a consequence of auto-catalysis,[3] the speed of the reaction being determined by the concentration of the acid and also by that of the hydrogen ions to which it gives rise by its electrolytic dissociation. If, at a given moment, the concentration of the non-esterified acid is $a - x$, and m is the degree of ionisation, then $m(a - x)$ is the hydrogen ion concen-

[1] Cf. Lapworth and Fitzgerald, *Trans. Chem. Soc.*, 1908, **93**, 2163; Lapworth, ibid., 2187; Lapworth and Partington, ibid., 1910, **97**, 19; Dawson, *Trans. Chem. Soc.*, 1911, **99**, 1; Bredig and Fraenkel, *Ber.*, 1906, **39**, 1756; Tubandt and Mohr, *Annalen*, 1907, **354**, 259.

[2] Cf. Lapworth, *loc. cit.*; Dawson, *loc. cit.*

[3] *Ber.*, 1896, **29**, 2208. In a later paper, *Zeit. f. Elektrochemie*, 1909, **15**, 4, Goldschmidt adopts the view that this reaction is of a secondary character, the primary reaction being due to the presence of very reactive double or complex molecules.

tration, and $dx/dt = k_2m(a-x)^2$. Assuming that m does not vary appreciably over the range of concentration involved, it is evident that the bimolecular velocity coefficient should remain constant during the reaction. The following data were obtained in an experiment with trichloracetic acid (0·2412 mol per litre) at 25°.

t (*hours*)	$a-x$	$\frac{1}{t}\frac{x}{a(a-x)}$
0	12·06	—
47·8	11·18	0.00676
118·0	10·24	0·00625
191·0	9·24	0·00663
291·0	8·30	0.00648
407·5	7·50	0.00618
672·0	6·07	0.00605

Although the numbers in the third column show that the bimolecular coefficient is practically constant, this constancy does not necessarily mean that the esterification, in absence of a catalyst, is auto-catalytic in nature, for it can be shown[1] that the same form of expression is obtained for the velocity coefficient, if it is assumed that the reaction takes place between the alcohol and the undissociated acid, or between the alcohol and the ions of the acid. In other words, the bimolecular nature of the process is a necessary consequence of the electrolytic dissociation of the acid.

Influence of the Nature and Constitution of the Acid on the Velocity of Esterification. From the work of numerous observers it has been possible to draw certain general conclusions relative to the influence of the nature and constitution of the acid on the velocity with which it is esterified in presence of a mineral acid catalyst. In the fatty series,[2] all substituted acetic acids are esterified more slowly than acetic acid itself, and in the series represented by (1) $CH_2X . CO_2H$; (2) $CHX_2 . CO_2H$; (3) $CX_3 . CO_2H$ it appears that the first is always more rapidly esterified than the second and the second more rapidly than the third. The velocity is independent of the strength of the acid, as measured by its ionisation constant in aqueous solution, and mainly depends on the number and 'size' of the atoms or groups which are substituted for hydrogen in the acetic acid. In the series of mono-substituted acetic acids, the methyl group has the smallest influence, the effect of other substituents increasing in the order—chlorine, phenyl, bromine, iodine (p. 340).

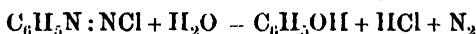
In the case of aromatic acids, similar retarding influences are apparent, and the effect of substitution in the ortho position is very

[1] Donnan, *Ber.*, 1896, 29, 2422.
[2] Sudborough and Lloyd, *Trans. Chem. Soc.*, 1899, 75, 467; 1898, 73, 81.

much greater than in the meta or para position. From experiments with the diortho substituted benzoic acids, it appears that certain of those are esterified with extreme slowness. That there is no real difference, however, between such diortho substituted acids and other substituted benzoic acids, such as the steric hindrance hypothesis would seem to suggest, is clearly shown by the fact that such diortho substituted acids can be esterified completely and without difficulty under favourable conditions (p. 340).[1]

In the absence of a mineral acid catalyst, the influence of substituting groups on the rate of esterification appears to be less sharply defined, and no very general relationships are exhibited by the dynamical data for auto-esterification.

Decomposition of Diazo-compounds. The decomposition of aqueous solutions of the diazo-compounds of the benzene and naphthalene series affords a further instance of a bimolecular reaction which proceeds in accordance with the equation for a unimolecular change.[2] In accordance with the equation



$$C_6H_5N:NCl + H_2O = C_6H_5OH + HCl + N_2$$

nitrogen is set free, and the progress of the reaction can be followed by collecting this nitrogen and determining the volume after measured time intervals.

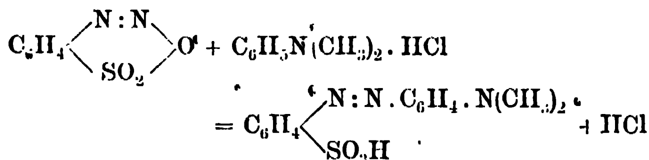
The velocities with which different diazo-compounds are decomposed vary enormously, as is evident from the following data, which express the relative velocities of decomposition, and afford therefore a measure of the relative stabilities of aqueous solutions of the diazo-compounds. In consequence of the great differences in the speed of decomposition, the diazo-compounds cannot all be compared at one and the same temperature, but, on the assumption that the temperature coefficients of the reaction velocities are sensibly the same, it is possible to refer the actual data to a common basis and so obtain a series of comparable numbers.

Relative Rates of Decomposition of Diazobenzene Compounds.

Diazo-o-nitrobenzene chloride	1
„ -m-nitrobenzene „	5.8
„ -p-nitrobenzene „	13.7
„ -p-sulphanilic acid	132
„ -p-toluene chloride	250
„ -benzene „	2200
„ -o-toluene „	6000
„ -m-toluene „	6500

[1] Rosanoff and Prager, *Journ. Amer. Chem. Soc.*, 1908, 30, 1895.
[2] Cain and Nicoll, *Trans. Chem. Soc.*, 1902, 81, 1412; 1903, 83, 206. Hantzsch, *Ber.*, 1900, 33, 2517; cf. also Hausser and Muller, *Bull. Soc. Chim.*, 1892 (111), 7, 721; 1893 (111), 9, 353.

Formation of Azo Colouring Matters. According to the equation

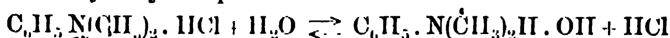


it might be expected that the reaction between p-diazobenzene-sulphonic acid and dimethylaniline hydrochloride would proceed at a rate determined by the product of the concentrations of the sulphonic acid and the aniline salt. When the experimental data are employed to calculate the bimolecular velocity coefficient, it is found, however, that the values vary considerably during the course of the reaction. Moreover, addition of hydrochloric acid to the solution lowers the speed to a considerable extent, and it is therefore improbable that the undissociated aniline salt or its ion represents one of the reacting components, for the active mass of these will not be appreciably altered by the addition of the acid.

If, on the other hand, it is assumed that the free base present in the solution is the active component, and if the concentration of this at any moment be denoted by ξ and the concentration of the sulphonic acid by $a-x$, then

$$dx/dt = k\xi(a-x). \qquad (1)$$

If, further, the original reaction mixture contains a mols of dimethyl-aniline hydrochloride and b mols of added hydrochloric acid per litre, then after time t, when x mols of the azo-compound have been formed, the concentrations of the hydrochloride, free base, and hydrochloric acid will be respectively $(a-\xi-x)$, ξ, and $(b+\xi+x)$ and from a consideration of the hydrolytic equilibrium



$$C_6H_5N(CH_3)_2 . HCl + H_2O \rightleftarrows C_6H_5 . N(CH_3)_2H . OH + HCl$$

it follows that

$$\frac{(\xi)(b+\xi+x)}{(a-\xi-x)} = K.$$

Since ξ can in general be neglected in comparison with $b+x$ and $a-x$, we may write

$$\xi = K\frac{a-x}{b+x},$$

and by substituting in equation (1)

$$dx/dt = kK\frac{(a-x)^2}{b+x},$$

or

$$kK = k' = \frac{1}{t}\left\{\frac{a+b}{a} \cdot \frac{x}{a-x} - ln\frac{a}{a-x}\right\}$$

In the following table are given the data obtained by Goldschmidt and Merz[1] in two experiments at 20° with different amounts of added acid.

a = 0·0282, b = 0·0282 *mol.*			a = 0·0282, b = 0·0564 *mol.*		
t (*minutes*)	$a-x$	k'	t (*minutes*)	$a-x$	k'
0	0·0282	—	0	0·0282	– –
45	0·0228	0·0057	90	0·0224	0·0060
150	0·0166	0·0057	210	0·0176	0·0056
210	0·0146	0·0057	375	0·0142	0·0061
300	0·0118	0·0063	480	0·0123	0·0063
390	0·0108	0·0058	1110	0·0068	0·0055
1320	0·0051	0·0056	1800	0·0058	0·0056

The retarding influence of the hydrochloric acid is seen from the fact that whereas the reaction is approximately half completed in 210 minutes in the first experiment, the time required for this in the second is about 375 minutes.

The constancy of k', as shown by the above numbers, together with the fact that neutral chlorides are without influence on the speed of the reaction, indicates with considerable certainty that the formation of methyl orange is due to the interaction of the diazo compound not with the aniline salt, but with the small quantity of free base which is present in the solution.

Transformation of Ammonium Cyanate into Carbamide. In the conversion of ammonium cyanate into carbamide in dilute aqueous solution, we have to deal with a reaction which is reversible to an extent which is easily measurable. The composition of the solution in the final condition of equilibrium indicates, however, that the velocity of decomposition of the carbamide may be almost neglected in comparison with the velocity of its formation, until at least 75 per cent. of the cyanate has been transformed, and, on this account, it is convenient to treat the reaction as belonging to the group of non-reversible changes. A further circumstance which complicates the process is the simultaneous decomposition of the cyanate with formation of ammonium carbonate, but this change may also be neglected in comparison with the principal reaction.

The following table contains data recorded by Walker and Hambly[2] for the decomposition of a 0·1 molar solution of cyanate at 50·1°. In calculating the uni- and bi molecular velocity coefficients (k_1 and k_2), the concentrations recorded under $a-x$ are reckoned from the practical end-point of the reaction which makes a = 0·0916 instead of 0·1.

[1] *Ber.*, 1897, 30, 670.
[2] *Trans. Chem. Soc.*, 1895, 67, 746.

t (*minutes*)	$a-x$	k_1	k_2
0	0·0916	—	—
45	0·0740	0·00206	0·0576
72	0·0656	0·00201	0·0599
107	0·0584	0·00183	0·0577
157	0·0512	0·00161	0·0548
230	0·0424	0·00145	0·0551
312	0·0343	0·00134	0·0572
600	0·0228	0·00101	0·0518

Whilst k_1 diminishes as the reaction proceeds, the values of k_2 are practically constant, indicating that the reaction is bimolecular. To account for this, it might be supposed (*a*) that two molecules of ammonium cyanate react together; (*b*) that the cyanate is dissociated into ammonia and cyanic acid, which yield carbamide by their interaction; (*c*) that the reacting components are the ammonium and cyanate ions or the non-ionised ammonium cyanate. Whereas the addition of neutral salts has, in general, no appreciable influence on the velocity of the reaction, it is found that ammonium salts increase the speed considerably. On the other hand, free ammonia, which is but feebly ionised in solution, has little influence on the rate of change. From these facts Walker and Hambly drew the conclusion[1] that the bimolecular course of the change is due to the interaction between the ammonium and cyanate ions, carbamide being formed from these as represented by



$$NH_4^{\cdot} + CNO' \rightarrow CO(NH_2)_2.$$

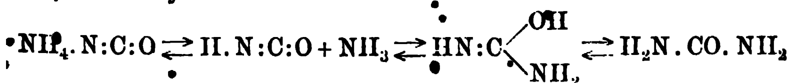
In agreement with this view it is found that k_2 diminishes somewhat as the initial concentration of the cyanate solution increases, this being due to the decrease in the ionisation of the salt as its concentration increases.

Most of these facts can be equally well interpreted, however, if we assume that it is the non-ionised portion of the ammonium cyanate which undergoes transformation, and the fact that in 90 per cent. ethyl alcohol, the cyanate is converted into carbamide thirty times as rapidly[2] as in pure water under similar conditions, is distinctly favourable to the view that non-ionised ammonium cyanate is the reactive substance.

According to Chattaway,[3] the transformation of the non-ionized cyanate into carbamide is not a case of simple intramolecular change, but is due to the interaction of ammonia and cyanic acid, analogous to the reactions between isocyanic esters and ammonia or

[1] For a criticism of this view compare E. E. Walker, *Proc. Roy. Soc.*, 1912, A 87, 539.
[2] Walker and Kay, *Trans. Chem. Soc.*, 1897, 71, 489.
[3] *Trans. Chem. Soc.*, 1912, 101, 170.

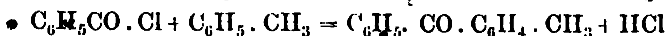
amines, whereby substituted carbamides are formed. The transformation may be formulated as follows:



$$NH_4.N:C:O \rightleftarrows H.N:C:O + NH_3 \rightleftarrows HN:C\begin{matrix}OH \\ NH_2\end{matrix} \rightleftarrows H_2N.CO.NH_2$$

and if this view is correct, the reaction in question belongs to the group of consecutive reactions (p. 313).

The Friedel-Crafts Reaction. Some light has been thrown on the mechanism of this general reaction by dynamical experiments. Steele[1] has investigated in this manner the formation of tolyl phenyl ketone from toluene and benzoyl chloride in presence of aluminium chloride and of ferric chloride (p. 195). The reaction corresponds with the equation

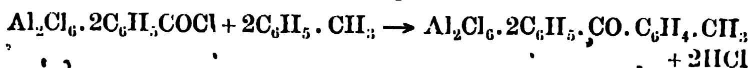


$$C_6H_5CO.Cl + C_6H_5.CH_3 = C_6H_5.CO.C_6H_4.CH_3 + HCl$$

and its progress was followed by passing a constant current of hydrogen, saturated with toluene vapour at the temperature of the experiment, through the reaction mixture and measuring the change in titre of a standard solution of alkali through which the issuing hydrogen, carrying the hydrogen chloride liberated by the reaction, was passed. In these experiments the toluene was present in large excess, and, under these circumstances, it might be expected that the reaction would be unimolecular. The experimental data show, however, that the order of the reaction varies with the ratio of the amounts of aluminium chloride and benzoyl chloride, being unimolecular if the ratio $AlCl_3/C_6H_5.COCl$ does not exceed unity, and bimolecular in presence of excess of aluminium chloride.

The results are best explained by assuming the formation of a compound between one or both of the reacting substances and the aluminium chloride, and by the removal of the latter from the system in combination with the ketone formed.

When the ratio $AlCl_3.C_6H_5CO.Cl$ does not exceed unity, the mechanism suggested by Perrier[2] and Bolseken[3] is sufficient to explain the dynamic observations. According to this, a compound is formed containing the acid chloride and aluminium chloride and this reacts with the toluene according to the formula



$$Al_2Cl_6.2C_6H_5COCl + 2C_6H_5.CH_3 \longrightarrow Al_2Cl_6.2C_6H_5.CO.C_6H_4.CH_3 + 2HCl$$

If this compound is only soluble to a limited extent in the

[1] *Trans. Chem. Soc.*, 1903, 83, 1470.
[2] *Ber.*, 1900, 33, 815.
[3] *Rec. trav. chim. Pays-Bas*, 1900, 19, 19; 1901, 20, 102.

toluene, the rate of change during the early stages of the reaction will be constant, because of the constant active mass of the compound in the saturated solution. The actual data show that the speed is constant until the aluminium chloride ceases to exist as a solid phase, and constant values are only obtained for the unimolecular velocity coefficient (k_1) if the time measurements are reckoned from the point at which this occurs.

That the aluminium chloride is removed from the reaction mixture in combination with the final product is indicated by the fact that one mol of aluminium chloride cannot convert more than one mol of the acid chloride into the ketone. If this were not the case, the regenerated aluminium chloride would react with further quantities of the acid chloride.

In order to account for the bimolecular character of the reaction in presence of excess of aluminium chloride, it is necessary to assume that this forms a similar additive compound with the toluene. The actual reacting components are then the two additive compounds, and the rate at which hydrogen chloride is evolved will be governed by the dynamic equation for a bimolecular change (coefficient = k_2).

The following tables contain data obtained by Steele in experiments under the two different conditions referred to above.

$AlCl_3$ 1·20 *gram.* $C_6H_5CO.Cl$ 1·18 *gram.* *Molar ratio* 1·0.
Toluene 20 *c.c.* x = HCl *liberated.*

t (*minutes*)	x	k_1	x/t
2·75	9·3	..	3·38
4·5	15·4	—	3·13
7·75	24.9	0·194	3·23
13·25	31·8	0·196	
16·0	33·4	0·200	
21·0	34·6	0·196	
26·0	35·1	0·195	
∞	35·4	—	

The numbers in the fourth column under x/t show that the speed is constant in the early stages, but the constancy of k_1 demonstrates the unimolecular character of the further progress of the reaction.

$AlCl_3$ 2·56 *gram.* $C_6H_5CO.Cl$ 1·18 *gram.* *Molar ratio*
Toluene 20 *c.c.* x = HCl *liberated.*

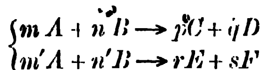
(*minutes*)	x	k_2
2·0	22·5	0·0229
3·0	26.4	0·0276
4·0	28·3	0·0281
5·0	29·2	0·0266
6·0	30·1	0·0269
7·75	31·3	0·0278
∞	35·4	—

Composite Reactions. In the reactions which have so far been discussed, it has been assumed that a single chemical change

is involved, that this proceeds in a particular direction and is moreover a direct process in the sense that the substances obtained are the immediate products of the interaction of the original substances. The majority of reactions do not satisfy these conditions, in that they usually involve simultaneous or consecutive changes, and, as a group, these reactions may conveniently be distinguished from the simple reactions by the term *composite reactions*.

To such composite reactions, an important principle applies the principle of mutual independence of different reactions—according to which, when a number of reactions occur simultaneously in any system, each of the component reactions proceeds in conformity with the mass law, and as if it were quite independent of the other reactions. We have in this principle a close analogy with that which determines the mechanical effect on a particle of the simultaneous application of a series of different forces. According to the nature of the component changes, composite reactions may be discussed under the head of concurrent, reversible, and consecutive reactions.

Concurrent Reactions. If the original substances A and B react together so as to give rise simultaneously to two series of products in accordance with the formula



$$\begin{cases} mA + nB \longrightarrow pC + qD \\ m'A + n'B \longrightarrow rE + sF \end{cases}$$

we have to deal with a case of two simultaneous concurrent reactions.

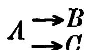
The general theory of such reactions has been discussed by Wegscheider.[1] In general, the ratio of the quantities of the different sets of products will be dependent on the time which has elapsed since the commencement of the reaction. If, however, the number of the molecules of each of the reacting substances involved is the same for the different concurrent reactions, the ratios of the products formed in the several processes will remain constant throughout the whole course of the reaction. In the example formulated above, the ratio of the quantities of the two series of products will be constant, provided $m = m'$ and $n = n'$.

In regard to the actual experimental investigation of reactions of this class, we are only concerned with those in which the concurrent reactions are limited to two or three, and where these are

[1] *Zeit. physik. Chem.*, 1899, 30, 593; cf. also Ostwald, *Lehrbuch*, 2, 2, 249; Mellor, *Chemical Statics and Dynamics*, p. 68.

of simple type (unimolecular or bimolecular). If we are dealing with two reactions, both unimolecular or both bimolecular, the quantities of the two sets of products will remain in a constant ratio, but this will not be the case if one reaction is unimolecular and the other bimolecular.

In the simplest case, where the two concurrent reactions are of the first order, as represented by



let a be the original quantity of A in unit volume, x the quantity transformed after time t, y and z the quantities of B and C formed after this time interval, and k_B and k_C the velocity coefficients of the two reactions, then we have

$$dx/dt = dy/dt + dz/dt \quad (1)$$

$$dy/dt = k_B(a - x) \quad (2)$$

$$dz/dt = k_C(a - x) \quad (3)$$

and therefore

$$dx/dt = (k_B + k_C)(a - x) \quad (4)$$

or on integration

$$k_B + k_C = \frac{1}{t} \ln \frac{a}{a - x} \quad (5)$$

which is identical with the equation for a simple unimolecular reaction.

In a similar manner, it can be shown that the integrated form of the equation for a pair of concurrent bimolecular reactions is of the same type as the corresponding equation for a simple bimolecular change.

From equations (2) and (3) we have

$$dy/dt \,/\, dz/dt = dy/dz = k_B/k_C = K \quad (6)$$

or the ratio of the quantities of the products of the two concurrent reactions is constant and equal to the ratio of the velocity coefficients.

From (5) and (6) it follows further that

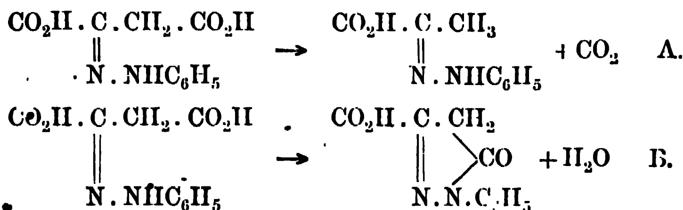
$$k_B = \frac{K}{K+1} \cdot \frac{1}{t} \ln \frac{a}{a - x} \quad (7)$$

and,

$$k_C = \frac{1}{K+1} \cdot \frac{1}{t} \ln \frac{a}{a - x} \quad (8)$$

and these equations furnish us with the velocity coefficients of the separate concurrent reactions. Examples of non-reversible changes of this type will now be considered.

Decomposition of Oxalacetic Acid Phenylhydrazone. The decomposition of pure aqueous or acidified solutions of oxalacetic acid phenylhydrazone, when heated at 100°, has been found by Jones and Richardson[1] to yield two different products—(A) pyruvic acid phenylhydrazone, (B) pyrazolonecarboxylic acid, as represented by the equations



Each of the two concurrent reactions is unimolecular, but the second differs from the first in that it appears to be catalytically accelerated by acids. In addition to the fact that relatively large quantities of pyrazolonecarboxylic acid are formed in mineral acid solutions as compared with pure aqueous solutions, reference may be made to the observation that solid oxalacetic acid phenylhydrazone yields only pyrazolonecarboxylic acid. Furthermore, it has been found that a given amount of the original substance yields less carbon dioxide as the amount of water in which it is dissolved diminishes, and that in other less strongly ionising solvents (such as pyridine, toluene), the relative amount of carbonic acid evolved is greater than in the case of aqueous solutions. All these facts agree with the assumption that reaction B is catalytically accelerated by the hydrogen ions resulting from the electrolytic dissociation of the acid hydrazones. If a is the amount of the oxalacetic hydrazone, originally present in unit volume of the solution, x the quantity decomposed after time t, y and z the quantities of pyruvic acid phenylhydrazone (or carbon dioxide) and pyrazolonecarboxylic acid formed, k_A and k_B the velocity coefficients of the reactions A and B, and H the concentration of the catalysing hydrogen ions, which is supposed to remain constant throughout the reaction, then

$$k_A + k_B . H = \frac{1}{t} ln \frac{a}{a-x}, \qquad (1)$$

and since $\qquad x = y + z \quad$ and $y\ z =$ constant,

therefore $\qquad x/y =$ constant and $x/z =$ constant.

If now the total amount of pyruvic hydrazone or carbon dioxide

[1] *Trans. Chem. Soc.*, 1902, 81, 1140.

formed, when the reaction is at an end, is represented by y_∞, then

$$a/(a-x) = y_\infty/(y_\infty - y)$$

and equation (1) may be written in the form

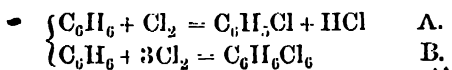
$$k_A + k_B . H = \frac{1}{t} ln \frac{y_\infty}{y_\infty - y} . \quad (2)$$

The progress of the reaction was actually followed by measurement of the volume of carbon dioxide evolved. The following table contains the data obtained in an experiment with a solution containing 0·1 gram oxalacetic acid phenylhydrazone in 100 c.c. of water.[1] The values under y represent the CO_2 evolved in c.c., y_∞ being equal to 320.

t (*seconds*)	y	$(k_A + k_B . H) . 10$
70	50	1·06
130	80	0·96
172	100	0·95
236	125	0·91
312	150	0·88
392	175	0·88
480	200	0·89
720	250	0·92

From experiments with sulphuric acid solutions containing from $\frac{1}{120}$ to $\frac{1}{10}$ equivalent of acid per litre it was possible to obtain the ratio of the coefficients k_B/k_A, and from this and the value of $(k_A + k_B . H)$ the separate velocity coefficients of the concurrent reactions could be determined. At 80° k_A was thus found equal to 0·000366 and k_B = 0·0183.

Chlorination of Benzene. When benzene is chlorinated in presence of iodine monochloride, substitution and addition occur simultaneously in accordance with the equations



$$\begin{cases} C_6H_6 + Cl_2 = C_6H_5Cl + HCl & A. \\ C_6H_6 + 3Cl_2 = C_6H_6Cl_6 & B. \end{cases}$$

This composite reaction has been followed dynamically by estimation of the quantity of unchanged chlorine and of the hydrogen chloride formed, the former affording a measure of the sum of the two velocities, the latter a measure of the velocity of reaction A. In pure benzene solution the course of the change was found to be in agreement with the equation for a unimolecular reaction, but experiments with solutions containing variable quantities of benzene dissolved in carbon tetrachloride showed that the speed of the

[1] Slator, *Trans. Chem. Soc.*, 1903, 83, 729.

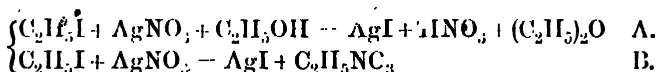
reaction is proportional to the benzene concentration. For given concentrations of chlorine and benzene the speed is moreover proportional to the square of the concentration of the catalyst, so that the rate of disappearance of chlorine may be represented by the equation

$$-\frac{d[Cl_2]}{dt} = kC_{Cl_2} \cdot C_{C_6H_6} \cdot C_{ICl}^2$$

At every stage during the reaction, the ratio between the amount of chlorine which enters the benzene nucleus and that which forms the hexachloride remains constant, this ratio being equal to 3·3. This observation shows that the two reactions are both unimolecular in presence of excess of benzene.

When stannic chloride or ferric chloride is employed as catalyst, the hexachloride is not formed to any appreciable extent, whereas reaction B is the only one which occurs under the influence of light. In all cases the course of the reaction is the same as in presence of iodine monochloride, the rate of disappearance of the chlorine being that required by the equation for a unimolecular reaction. The differences in the relative quantities of the two products show, however, that the relative speeds of the concurrent reactions may be altered to a very large extent by suitable variation of the catalyst.

Action of Silver Salts on Alkyl Iodides. When silver nitrate acts on ethyl iodide in absolute alcoholic solution, two changes occur simultaneously, as represented by the equations[1]



$$\begin{cases} C_2H_5I + AgNO_3 + C_2H_5OH = AgI + HNO_3 + (C_2H_5)_2O & \text{A.} \\ C_2H_5I + AgNO_3 = AgI + C_2H_5NO_3 & \text{B.} \end{cases}$$

Experiments at 25° show that the proportion of silver nitrate which reacts according to A amounts to 70 per cent., and that this proportion holds good for the entire course of the change. From this it may be inferred that the reactions are concurrent and of the same order.

The rate at which the silver nitrate disappears in any given experiment is in quite satisfactory agreement with the assumption that the reaction is bimolecular, as might be anticipated from the chemical equations. When, however, the initial concentration of the reacting substances is increased, the velocity coefficient also increases, and from this it may be inferred that the reaction is

[1] Burke and Donnan, *Trans. Chem. Soc.*, 1904, 85, 555; *Zeit. physik. Chem.*, 1909, 69, 115.

not really of the second order. The change in magnitude of the velocity coefficient is chiefly due to the silver nitrate, for, in experiments with constant silver nitrate and increasing ethyl iodide concentration, slightly falling values are obtained for k_2. The observed constancy of k_2 throughout any one experiment is therefore due, in all probability, to the formation of some substance during the reaction which has an accelerating effect on the velocity of the change. Of the main products of the reaction, ethyl nitrate and ethyl ether are inactive, and nitric acid diminishes the velocity. On the other hand, the speed is increased when nitrates are added to the reaction mixture, although these substances produce no alteration in the ratio of the two sets of products A and B. From this it might be inferred that the undissociated silver nitrate is the particular component which reacts with the alkyl iodide, for addition of nitrates will diminish the concentration of the silver ion and increase that of the undissociated salt.

When silver lactate is substituted for the nitrate,[1] the chemical nature of the change undergoes no alteration, the ratio of the quantities of the two sets of products being the same for lactate as for nitrate. In the case of the lactate, however, the accelerating effect referred to is absent, and the values of the bimolecular velocity coefficient fall as the reaction proceeds.

If it is assumed that the reaction takes place between the ethyl iodide and the undissociated silver salt, the rate of change at any moment may be written

$$dx/dt = k(1 - \alpha)(a - x)^2 \qquad (1)$$

where a is the original concentration of both silver salt and alkyl iodide and α the degree of electrolytic dissociation of the silver salt.

Assuming further that the ionisation varies with the concentration in accordance with the mass law,

then

$$\frac{\alpha^2}{1 - \alpha}(a - x) = K, \qquad (2)$$

and from (1)

$$dx/dt = \frac{k}{K}\alpha^2(a - x)^3 = k_3(a - x)^3 \qquad (3)$$

Although α is not very different from unity at the dilutions employed in the dynamic experiments, it will increase slightly as the reaction proceeds, and in consequence $k_3 = \frac{k}{K}\alpha^2$ may be expected

[1] Donnan and Potts, *Trans. Chem. Soc.*, 1910, 97, 1882.

to increase somewhat during the reaction. The following data show that this is actually the case :

t (minutes)	0	4·2	11·1	30·1	48·5	84·7	119·0
$a-x$	2·89	2·0	1·50	1·00	0·80	0·60	0·50
k_3	—	0·030	0·028	0·029	0·031	0·033	0·035

The velocity equation assumes the same form if we suppose that the iodide reacts only with the ions of the silver salt, but the increased speed of the reaction which is observed on the addition of nitrates to the mixture of ethyl iodide and silver nitrate indicates that the active agent is represented by the undissociated silver salt.

In view of the attempts which have been made in recent years to refer organic reactions to interactions of ions, this result is of special interest, for the reaction between an ionised salt and an organic halogen compound may be regarded as one in which the conditions are favourable to interionic action.

Although it might be expected that the velocities of reaction between silver nitrate and the iodo-derivatives of methane would exhibit a regular gradation, experiment shows that this is not the case. The velocity coefficient for iodoform is about one-eighth of that of methyl iodide, and the reactivity of methylene iodide, instead of having an intermediate value, is only about one-hundredth of that of iodoform.

Formation of Disubstitution Products of Benzene. The nitration, sulphonation, and halogenation of mono-substituted benzene derivatives affords an instance of a general reaction in which three concurrent changes are involved, giving rise to the formation of ortho-, meta-, and para-disubstitution products. Although no satisfactory explanation has been given of the marked tendency towards the production of disubstitution products belonging to one or other of these groups, it is evident that the relative amounts of the three products in a particular case are determined by the velocities with which the corresponding reactions occur under a given set of conditions. By variation of the conditions (temperature, concentration, reaction medium) the relative amounts undergo variation, and this must be due to differences in the extent to which the velocities of the three reactions are affected.

Although no reaction of this kind has been examined in detail, the relative amounts of the products formed under different conditions have been investigated for the nitration of benzoic acid and its methyl and ethyl esters.[1] The proportions of the nitro-

[1] Holleman, *Zeit. physik. Chem.*, 1899, 31, 79.

substitution products must be in the ratio of the rates of formation and therefore of the respective velocity coefficients k_o, k_m, and k_p for the ortho-, meta-, and para-compounds, the progress of the reaction being given by the equation

$$dx/dt = (k_o + k_m + k_p)(a - x)$$

if the nitric acid is present in large excess.

In experiments at different temperatures, Holleman obtained the following percentage proportions for the three nitro-benzoic acids:

Temperature.	*Ortho.*	*Meta.*	*Para.*
−30°	14·4	85·0	0·6
0°	18·5	80·2	1·3
+30°	22·3	76·5	1·2

Reversible Reactions. If the products of a chemical change react together with the formation of the original substances, and if this reverse change occurs, under the conditions of the direct reaction, with a velocity which is of the same order of magnitude, the reaction in question belongs to the type of opposing, balanced, reversible, or counter reactions. The principle of the mutual independence of different reactions applies to such a case just as to a series of concurrent reactions. Each of the independent reactions has its speed determined by a certain velocity coefficient, by the active masses of the molecular species concerned, and by the number of molecules which are involved in the actual process of interaction.

As compared with a non-reversible reaction of the same order, the apparent speed of such a reversible change falls off more quickly as the original substances disappear, because of the fact that these substances are continuously regenerated from the reaction products. The velocity of the opposed reaction increases with the accumulation of the products of change, and since that of the direct reaction diminishes during this process, a point will ultimately be reached where the velocities of the two opposed reactions are equal to one another. When this condition has been attained the system is said to be in equilibrium, and, so long as the external conditions are unaltered, the quantities of the original and final products present will remain absolutely constant. If the reacting substances are mixed at the outset with the final products in such quantities as correspond with the equilibrium condition, no change will take place. The so-called equilibrium constant is simply the ratio of the velocity coefficients of the opposing reactions, and as such its evaluation affords but little information in regard to the mechanism of the two opposing reactions.

Amongst the many examples of reversible reactions which have been investigated dynamically, those in which the opposing reactions are both unimolecular belong to the simplest type. If such a reaction is represented by the formula



and if a be the quantity of A originally present in unit volume (B being absent), x the quantity of A decomposed and therefore of B formed after time t, k_1 and k_1' the velocity coefficients of the direct and reverse reactions, then the rate at which A disappears is given by

$$dx/dt = k_1(a-x) - k_1'x. \tag{1}$$

When the state of equilibrium is attained $dx/dt = 0$, and if the corresponding value of x is ξ, then $k_1(a-\xi) = k_1'\xi$

or

$$\frac{k_1}{k_1'} = K = \frac{\xi}{a-\xi}, \tag{2}$$

where K is the equilibrium constant.

From (1) and (2) we obtain

$$\frac{1}{k_1'}\frac{dx}{dt} = K(a-x) - x,$$

and by integration

$$k_1 + k_1' = \frac{1}{t} \ln \frac{Ka}{Ka - (K+1)x}. \tag{3}$$

Since $K = k_1/k_1'$, this equation may be written so as to give the values of the individual velocity coefficients, and we then obtain

$$k_1 = \frac{K}{K+1}\frac{1}{t}\ln\frac{Ka}{Ka-(K+1)x}, \quad k_1' = \frac{1}{K+1}\frac{1}{t}\ln\frac{Ka}{Ka-(K+1)x}. \tag{4}$$

By substitution of

$$K = \frac{\xi}{a-\xi} \text{ in (4),}$$

we obtain

$$k_1 = \frac{\xi}{a}\frac{1}{t}\ln\frac{\xi}{\xi - x} \quad \text{and} \quad k_1' = \frac{a-\xi}{a}\frac{1}{t}\ln\frac{\xi}{\xi-x}, \tag{5}$$

and from these

$$k_1 + k_1' = \frac{1}{t}\ln\frac{\xi}{\xi - x}. \tag{6}$$

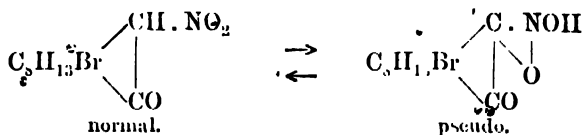
It should be observed that equation (6) bears a close resemblance to the equation for an irreversible unimolecular change. The only difference is that the expression on the right-hand side of (6) contains the quantity of the original substance which has disappeared when the condition of equilibrium is attained, in place of the quantity of this substance which was initially present. If k_1' is small in

comparison with k_1, then ξ will not be very different from a and the equation for the reversible reaction passes over into that for the irreversible change.

If the opposing reactions are both of the second order, or if one of them is unimolecular and the other bimolecular, it is possible by a similar procedure to deduce equations in which x and t are expressed in terms of the velocity coefficients of the two opposed reactions, but these more complex cases will not be considered here from a general standpoint.

Dynamic Isomerism of Nitro-camphor and its Derivatives.[1] Solutions of nitro-camphor or other secondary nitro-derivatives of camphor exhibit the phenomenon of mutarotation. The progressive change in rotatory power appears to depend on a particular grouping in the molecule, for the mutarotation occurs in all solvents. It is probable therefore that the change involved is an intramolecular transformation which is independent of any chemical interaction between the nitro-camphor and the solvent (Part II, p. 348).

In the case of π-bromonitro-camphor, both isomers or isodynamic forms have been isolated. The normal form melts at 108°, and has a rotatory power $[\alpha]_D = -51°$ in 3·33 per cent. benzene solution at 13°. The pseudo form melts at 142° and its rotatory power $[\alpha]_D = +188°$ in 3·33 per cent. benzene solution at 15°. These rotation values have reference to the freshly prepared solutions only; for each solution changes gradually in its rotatory power and in each case the same final rotation is obtained $[\alpha]_D = +38°$. This then is the rotatory power of an equilibrium mixture of the two isodynamic forms, the equilibrium condition resulting from the equality of the speeds of the opposed reactions represented by



Measurement of the rotation of the solution after suitable time intervals enables the progress of the reaction to be followed very conveniently. If r_0 denotes the initial rotation of a solution of the pseudo form, r the rotation after time t, and r_∞ the equilibrium rotation, then, since x is proportional to $(r_0 - r)$ and ξ to $(r_0 - r_\infty)$, we may write

$$k_1 + k_1' = \frac{1}{t} \ln \frac{\xi}{\xi - x} = \frac{1}{t} \ln \frac{r_0 - r_\infty}{r - r_\infty}.$$

[1] Lowry, *Trans. Chem. Soc.*, 1899, 75, 211; *B. A. Report*, 1904.

In the following table are recorded the results obtained with a 5 per cent. solution of pseudo π-bromonitro-camphor in chloroform solution at 14°.[1]

t (*hours*)	*r*	$\frac{1}{t}\log_{10}\frac{r_0-r_\infty}{r-r_\infty}$
0·2	+188·3	—
3·0	169·0	0·0197
5·0	156·0	0·0198
7·0	146·0	0·0198
24·0	84·5	0·0197
72·0	37·3	0·0197
81·0	35·8	0·0191
96·0	34·0	0·0184
∞	31·3	—

The concordance of the numbers in the third column affords satisfactory evidence of the correctness of the view that the muta-rotation is due to reversible isodynamic change. Whether or no the transformation of the pseudo or the normal form is subjected to dynamic investigation, it is obvious that the value of $k+k'$ should be the same. In this particular case, actual experiment gave divergent values, for whereas k_1+k_1' was found to be 0·0188 from observations of the rate of transformation of a 3·33 per cent. benzene solution of the pseudo form, the corresponding value calculated from the data for the normal form was only 0·0064. It is very probable that the difference in the two values is due to secondary disturbances, for the isodynamic change in question has been shown to be extremely sensitive to traces of impurities.

In solvents which contain oxygen the velocity of the isomeric transformation is much greater than in hydrocarbons, carbon disulphide, or chloroform. Bases like piperidine in chloroform and benzene solution, and sodium ethoxide in ethyl alcohol, accelerate the change enormously. Neutral salts also exert an accelerating effect although of much smaller magnitude, and the influence of acids is still less marked.

In general, the isodynamic change begins as soon as the substance is brought into solution, but anomalous results have been found in certain cases.[2] In chloroform solution, for example, normal nitro-camphor was found to be comparatively stable; this was afterwards found to be due[3] to the presence of small quantities of carbonyl chloride (formed by oxidation of the chloroform) which converts any traces of ammonia or other aminic impurities into inert carbamides and so destroys their catalytic action. By the addition of

[1] Lowry, *loc. cit.*
[2] Lowry and Magson, *Trans. Chem. Soc.*, 1908, 93, 107.
[3] Lowry and Magson, *Trans. Chem. Soc.*, 1908, 93, 119.

small quantities of carbonyl chloride (or other acid chlorides), the isodynamic change can also be arrested in other solvents.

From his observations on the isodynamic change of the secondary nitro derivatives of camphor, Lowry assumes that the presence of a catalyst is necessary before the change can occur. Such changes, which belong to the keto-enol type, are brought about by substances, all of which may be represented by the general formula *HX*, such as water, alcohols, acids, amines, and bases, and the way in which these act is supposed to be by the formation of addition compounds, from which the catalyst may be eliminated in a different way from that in which it entered into combination with the original substance.

Mutarotation of the Mono-saccharoses.[1] The mutarotation phenomena exhibited by the mono-saccharoses are closely similar to those which have been referred to in the preceding section. The α- and β-forms of glucose represent isodynamic modifications, and their aqueous solutions exhibit gradual changes in rotatory power, the ultimate rotation being the same independently of whether the original solution was prepared by dissolving the α- or the β-form. The equilibrium mixture corresponds with what was at one time supposed to be a third modification of glucose (Part III, p. 44).[2]

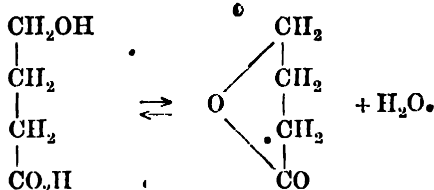
Lactose shows exactly similar relationships, and from Erdmann's observations[3] on the rates of change of the two isomeric forms, it has been found[4] that $(k_1 + k_1')$ has the same value whether the sum of the velocity coefficients is calculated from the direct or the reverse reaction. This is shown by the following data:

Solution of α-lactose.			*Solution of β lactose.*		
t (*minutes*)	r	$k_1 + k_1'$	t (*minutes*)	r	$k_1 + k_1'$
0	84·0°	—	0	39·5°	—
60	73·4°	0·00206	60	45·8°	0·00209
120	67·3°	0·00197	120	49·6°	0·00206
180	62·9°	0·00203	180	52·2°	0·00212
240	60·1°	0·00209	240	53·9°	0·00224
∞	56·0°	—	∞	56·0°	—
	Mean	0·00204		Mean	0·00213

Within the limits of experimental error, the mean values of $k_1 + k_1'$ are identical, and the requirements of theory are therefore fully satisfied in this important particular.

[1] Cf. Urech, *Ber.*, 1882, 15, 2130; 1883, 16, 2270; 1884, 17, 1547; 1885, 18, 3047.
[2] Lowry, *Proc. Chem. Soc.*, 1904, 20, 108; Tanret, *Bull. Soc Chim.*, 1871 15. 195, 849; 1872, 17, 802.
[3] *Ber.*, 1880, 13, 2180.
[4] Hudson, *Zeit. physik. Chem.*, 1903, 44, 487.

Formation of Lactones from γ- and δ-Hydroxy Acids. In presence of mineral or other strong acids, γ-hydroxybutyric acid is partially converted into the corresponding lactone, the reaction being reversible, as represented by the formula



Whereas the dehydration of the acid appears to be a unimolecular process, the hydration of the lactone involves the interaction of two molecules and is therefore bimolecular. Since the water is present in large excess, however, its active mass remains practically constant, and on this account the hydration may be expected to proceed in accordance with the equation for a unimolecular change. In presence of a sufficient quantity of mineral acid, which accelerates both reactions to exactly the same extent since it is without influence on the final equilibrium, the reaction takes place at a convenient speed at the ordinary temperature and can be followed by titration of the unchanged acid by means of a standard solution of alkali. The following data were obtained by Henry[1] in an experiment at 25° with a solution containing initially 0·1767 mol γ-hydroxybutyric acid per litre, normal hydrochloric acid being used as catalyst:

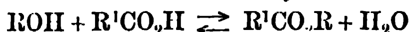
t (*minutes*)	x (*in c.c. of alkali solution*)	$k_1 + k_1'$
0	0	—
21	2·41	0·0355
50	4·96	0·0374
65	6·10	0·0382
100	8·11	0·0381
160	10·35	0·0382
220	11·55	0·0370
∞	13·28 = ξ	—

In the absence of an acid catalyst, γ-hydroxy acids are also slowly converted into the corresponding lactones under the influence of the hydrogen ions which are formed by their own electrolytic dissociation. Under these circumstances, the change affords an instance of an auto-catalysed reaction, and on the assumption that the opposing reactions are accelerated in proportion to the concentration of the hydrogen ions and that it is the undissociated acid which undergoes dehydration, it is possible to obtain an expression for the progress of the change

[1] *Zeit. physik. Chem.*, 1892, 10, 96.

which is also in satisfactory agreement with experimental observations (compare Henry, *loc. cit.*).

Esterification. The formation of an ester from the corresponding alcohol and acid affords an example of a reversible bimolecular change, as might be expected according to the formula



$$ROH + R'CO_2H \rightleftarrows R'CO_2R + H_2O$$

When esterification or ester hydrolysis occurs in aqueous alcoholic solutions under the influence of an acid catalyst, the active masses of the alcohol on the one hand, and of the water on the other, remain unaltered during the progress of the reaction, and in accordance with this it has been found that both esterification and ester hydrolysis proceed at a rate which can be calculated from the equation for a reversible unimolecular change.

The following data were obtained by Kistiakowsky[1] for the esterification of formic acid in 41 per cent. alcoholic solution at 24·75°.

Formic acid, 0·0668 *mol per litre.*		HCl, 0·0262 *mol per litre.*	
t (*minutes*)	*x* (*in c.c. of alk.*)	k_1	k_1
0	0	–	—
30	1·26	62	106
70	2·72	62	106
110	4·07	63	107
150	5·29	61	105
210	7·10	64	110
330	8·92	63	107
∞	11·48		

When ethyl formate is hydrolysed under the same conditions, values of k_1 and k_1' are obtained which are equal to those recorded in the above esterification experiment.

From the previous discussion of esterification and ester hydrolysis (see pp. 279, 290) it appears that ester hydrolysis in aqueous solution and esterification in alcoholic solution are changes which in presence of an acid catalyst take place in agreement with the equation for a non-reversible unimolecular reaction, whilst in aqueous alcoholic solutions both changes proceed in accordance with the requirements of the equation for a reversible unimolecular reaction. When none of the reacting substances is present in large excess, the dynamical course of both esterification and ester hydrolysis can only be represented by the equation for a reversible bimolecular reaction.

If equimolecular quantities of ethyl alcohol and acetic acid are mixed together and the volume containing the gram molecular

[1] *Zeit. physik. Chem.* 1898, 27, 250.

quantity of each is taken as unit volume, then the rate of ester formation will be given at any moment by the equation

$$dx/dt = k_2(1-x)^2 - k_2' x^2. \qquad (1)$$

Since equilibrium is attained when almost exactly two-thirds of the reacting substances have been transformed into ester and water, it follows that

$$K = \frac{k_2}{k_2'} = \frac{x^2}{(1-x)^2} = 4 \cdot 0. \qquad (2)$$

By making use of (2) in the integration of (1) we obtain the relationship

$$k_2 = 4k_2' = \frac{1}{t} ln \frac{2-x}{2-3x}. \qquad (3)$$

The following table records the observations of Berthelot and Saint-Gilles[1] on the speed of ester formation at the ordinary room temperature; from these data are calculated the values of the coefficient $k_2 = 4k_2'$.

t (days)	0	19	41	64	103	137	167	190	∞
x	0	0·121	0·200	0·250	0·315	0·421	0·474	0·496	0·677
$k_2 = 4k_2'$	—	0·0072	0·0061	0·0053	0·0052	0·0056	0·0058	0·0057	—

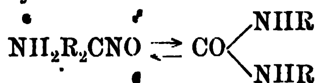
From the series of k_2 values, it appears that the observed course of the reaction is in satisfactory agreement with theory except in the initial stages. The apparent diminution of the speed during this part of the reaction is perhaps connected with the influence of the water, initially formed, on the properties of the acid, and, if so, the effect is analogous to that which has been already noted in the case of esterification in absolute alcoholic solution.

According to Knoblauch's experiments[2] the same values are obtained for the velocity coefficients k_2 and k_2' independently of whether these are deduced from observations on the speed of esterification or of ester hydrolysis.

Conversion of Alkyl Ammonium Cyanates into the corresponding Carbamides. Although the formation of carbamide from ammonium cyanate has been discussed on p. 295 as a bimolecular non-reversible change, this can only be justified on the ground that the speed of the reverse reaction is relatively small. In the case of certain of the alkyl ammonium cyanates[3] the difference in the velocities of the opposed reactions is not nearly so large, and it becomes necessary to take the reverse transformation into account.

[1] *Ann. Chim. Phys.*, 1862 (3), 65, 385; 1862 (3), 66, 5; 1863 (3), 68, 225.
[2] *Zeit. physik. Chem.*, 1897, 22, 268.
[3] Walker and Appleyard, *Trans. Chem. Soc.*, 1896, 69, 193.

For a dialkyl ammonium cyanate we have therefore a reversible reaction represented by



the speed of formation of the carbamide at any moment being given by

$$dx/dt = k(a-x)^2 - k'x$$

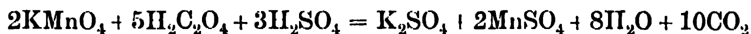
By integration of this and the relation between k and k' which is afforded by the state of equilibrium, namely $K = k/k' = \frac{\xi}{(a-\xi)^2}$, k and k' may be evaluated in terms of a, ξ, x, and t, and experiment shows that the decomposition of the alkyl ammonium cyanates can be adequately accounted for on the assumption that the actual change is the resultant of two opposed reactions, one of which is bimolecular and the other unimolecular.

In the appended table are given the values of k and k' for a series of alkyl derivatives:

Cyanate	$100k$	$100k'$	k/k'
Ammonium	11·4	0·0038	3800
Methyl ammonium	13·4	0·0022	6100
Dimethyl ,,	25·3	0·073	350
Ethyl ,,	8·1	0·007	1150
Diethyl ,,	9·0	0·148	60
*Iso*amyl ,,	9·2	0·0031	3000
Ter-amyl ,,	1·3	0·04	32

On comparing the values of k/k' for the dialkyl and the corresponding mono-alkyl derivatives it is seen that the relative speed of the reverse change is much greater for the former than for the latter. In agreement with this is the fact that carbamides are not formed to any appreciable extent from the tri-alkyl and tetra-alkyl ammonium cyanates.

Consecutive Reactions. In many reactions the number of reacting molecules, which is indicated by the dynamical data, is quite different from that which corresponds with the chemical equation. According to the equation for the oxidation of oxalic acid by potassium permanganate in presence of sulphuric acid,

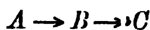


$$2KMnO_4 + 5H_2C_2O_4 + 3H_2SO_4 = K_2SO_4 + 2MnSO_4 + 8H_2O + 10CO_2$$

it might be supposed that ten molecules $(2+5+3)$ are involved in the intermolecular transaction by which the final products are obtained. In general, however, the velocity curves of complicated reactions of this character can only be satisfactorily interpreted on the assumption that the actual change which determines the velocity

is of a simple character, that is to say, of the first, second, or possibly the third order. Hence it seems probable that such reactions take place in two or more stages and belong to the group of consecutive reactions.

Such consecutive changes will exhibit differences according to the number, the relative speeds, and the orders of the successive stage reactions and also according to whether the component reactions are reversible or irreversible. Except in comparatively simple cases, the mathematical analysis of the dynamics of such composite reactions is of a complicated character, and in this chapter no attempt will be made to consider more than the simplest possible case, namely, that of a reaction taking place in two stages, each of the component reactions being irreversible and unimolecular. Such a change may be represented by the formula



$$A \longrightarrow B \longrightarrow C$$
$$(1) \quad (2)$$

If, initially, a mols of A are present in unit volume, and after time t the quantities of A, B, and C present are x, y, and z respectively, and if k_1 and k_2 are the velocity coefficients of the first and second reactions, then, according to the mass law,

the rate of disappearance of A is

$$-\frac{dx}{dt} = k_1 x \text{ or } x = ae^{-k_1 t}, \qquad (1)$$

the rate of formation of C is

$$\frac{dz}{dt} = k_2 y, \qquad (2)$$

and the rate at which B accumulates is

$$\frac{dy}{dt} = -\frac{dx}{dt} - \frac{dz}{dt} = k_1 x - k_2 y. \qquad (3)$$

Further, we have the relationship

$$x + y + z = a, \qquad (4)$$

and from equations (1) to (4) it can be shown that

$$z = a - \frac{a}{k_1 - k_2}(k_1 \cdot e^{-k_2 t} - k_2 \cdot e^{-k_1 t}), \qquad (5)$$

in which the quantity z of the final product, which has been formed after any given time interval t, is expressed in terms of the initial concentration (a) of the original substance and the velocity coefficients k_1 and k_2 of the two consecutive reactions.

By analysis of equation (5) it can be readily shown that if the

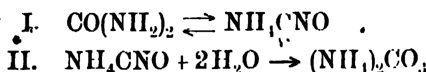
velocity coefficient of one of the component reactions is very much larger than that of the other, the rate at which C is formed will be determined by the speed of the slow reaction. Without reference to equation (5), however, it is quite obvious that, under these circumstances, the speed of the entire change will be determined solely by that of the relatively slow component, and that the rapid component reaction will be without measurable influence. Under these conditions it is to be expected that the progress of the consecutive reaction will be the same as that of a simple reaction of the same order. In many cases, in fact, it may not be possible to distinguish the composite from the simple reaction, although a distinction may be easily drawn in others. If the first stage in the change $A \longrightarrow B \longrightarrow C$ is relatively very slow, the rate at which C is formed will be practically the same as the rate at which A disappears, and the formation of the intermediate substance may be masked. On the other hand, if the first stage is relatively very rapid, the formation of the intermediate substance becomes very obvious, although the isolation of it from the reaction mixture may not be feasible.

If the velocity coefficients of the successive reactions are of the same order of magnitude, the relationships are much more complicated. So far as the original substance A is concerned the matter is quite simple, for this will disappear in accordance with the equation for a non-reversible unimolecular change. On the other hand, the rate at which C is formed depends on the concentration of the intermediate substance B, and this is obviously dependent on the speeds of the two reactions. If the quantities of A, B, and C present in the mixture are plotted as a function of time, the curve for A falls continuously, that representing C rises, but the B curve first rises and then falls, passing through a maximum. As the quantity of B increases from zero at the commencement of the reaction to its maximum value, the rate of formation of the final product increases correspondingly, and attains a maximum when B is at its maximum; thereafter the rate of formation gradually falls off. The point at which the velocity of formation of the final product reaches its maximum value is clearly dependent on the relation between the speeds of the two successive reactions.

Decomposition of Carbamide by Acids and Alkalis. An example of a consecutive reaction is afforded by the hydrolytic decomposition of carbamide, investigated in detail by Fawcett[1] by experiments in sealed tubes at the temperature of boiling water.

[1] *Zeit. physik. Chem.*, 1902, 41, 601.

The first stage consists in the formation of ammonium cyanate, which, in the second, is converted into ammonium carbonate in accordance with the formulae



$$\text{I.}\quad CO(NH_2)_2 \rightleftarrows NH_4CNO$$
$$\text{II.}\quad NH_4CNO + 2H_2O \rightarrow (NH_4)_2CO_3$$

From determinations of the ammonia present after different time intervals, it appears that the final product is formed at a rate which can be calculated from the equation for a simple unimolecular change. This is the case whether the solution is acid, alkaline, or neutral, but the magnitude of the velocity coefficient varies considerably according to the nature of the solution, as is shown by the data in the following table :

Hydrolysis of $\frac{1}{8}$ normal carbamide.

Nature of solution	$k_1 = \frac{1}{t} \log_{10} \frac{a}{a-x}$
$\frac{1}{10}$ normal HCl	102×10^{-5}
$\frac{1}{8}$ normal NaOH	60×10^{-5}
Neutral	$6{\cdot}8 \times 10^{-5}$

In presence of acids, the intermediate substance, ammonium cyanate, is decomposed very rapidly, but more slowly in presence of alkali hydroxides. In neutral aqueous solution the velocity cannot be determined, because of the fact that the cyanate is almost completely converted in a very short time into carbamide in accordance with the equation for reaction I. Since, however, potassium cyanate is decomposed with considerable speed into potassium carbonate and ammonia in neutral solution, it is reasonable to infer that ammonium cyanate will be decomposed with appreciable velocity under similar conditions.

If the original solution of carbamide contains a mols per litre, and if x mols have been decomposed after time t, the speed of carbamide decomposition at this moment will be given by

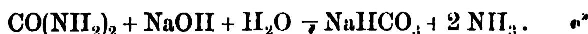
$$dx/dt = k_1(a-x) - k_1' x^2$$

where k_1 and k_1' are the coefficients of the opposed reactions in I. Since in acid solution the cyanate is decomposed at a relatively very rapid rate, the actual concentration of the cyanate must be very much smaller than x, and in consequence the second term on the right-hand side of the equation may be neglected. In dilute acid solution the speed of the reaction will therefore be determined by the velocity coefficient k_1 of the reaction



$$CO(NH_2)_2 \rightarrow NH_4CNO.$$

In pure aqueous solution, where the velocity of decomposition of the cyanate is much smaller than in presence of acid, the effective rate at which carbamide is transformed will be diminished in consequence of the accumulation of ammonium cyanate and its reconversion into carbamide. It is probable that this operates to some extent in alkaline solution (compare previous table), but a further complication arises here in that the carbamide appears to be directly hydrolysed by solutions of alkali hydroxide without the intermediate formation of ammonium cyanate, as represented by the equation



$$CO(NH_2)_2 + NaOH + H_2O = NaHCO_3 + 2\,NH_3.$$

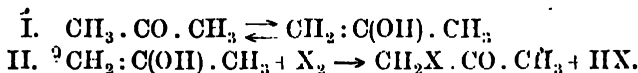
In agreement with this, it is found that the speed of the reaction in strongly alkaline solutions is much greater than in acid solutions, that is to say, greater than corresponds with the velocity coefficient k_1. The hydrolysis of carbamide by solutions of the alkali hydroxides is therefore a rather complex process, involving two concurrent reactions (direct and indirect hydrolysis), one of which takes place in successive stages.

Action of Halogens on Carbonyl Compounds. In reference to the mechanism of the process of substitution of hydrogen in certain compounds by halogens, experimental evidence is available which indicates that in the case of compounds containing the group :CH.CO, e.g. ketones, aldehydes, carboxylic acids and their derivatives, the substitution is not the result of a simple process but of one in which two or more successive reactions are involved. As a general rule, those carbonyl compounds are the most easily attached which are known to be capable of conversion into their enolic forms. In the comparable case of the nitro-paraffins it has also been observed that these are not capable of being brominated directly, but are easily converted into bromo-derivatives if first transformed into the isonitro form, corresponding with the enolic form of carbonyl compounds.

In presence of a mineral acid, the aliphatic ketones react with the halogens in dilute aqueous solution at a rate which can be followed conveniently at the ordinary temperature. When the ketone is present in large excess, the halogen disappears at a constant rate, which is proportional to the concentration of the ketone and the acid, but is independent of the concentration of the halogen.[1] The fact that the velocity remains unaltered, as the halogen disappears from the reaction mixture, indicates that the speed of the halogenation process is determined by a preliminary reaction in which the

[1] Lapworth, *Trans. Chem. Soc*, 1904, 85, 30; Dawson and Leslie, *Trans. Chem. Soc.*, 1909, 95, 1860.

halogen is not directly concerned. It is therefore supposed that the first stage consists in the transformation of the ketone from the ketonic to the enolic form, and that this change is catalytically accelerated by the acid. This slow isomeric change is then succeeded by a relatively very rapid change, in which the enolic ketone reacts with the halogen X in accordance with the formulae



$$\text{I.}\quad CH_3.CO.CH_3 \rightleftarrows CH_2:C(OH).CH_3$$
$$\text{II.}\quad CH_2:C(OH).CH_3 + X_2 \longrightarrow CH_2X.CO.CH_3 + HX.$$

In support of this view it may be mentioned that the speed of the reaction is practically independent of the nature of the halogen. This is to be expected if reaction II is a relatively very rapid change, for the disappearance of the halogen will be determined by the velocity coefficient of the reaction $CH_3.CO.CH_3 \longrightarrow CH_2:CO.CH_3$, and, if the active mass of the acetone is practically constant, this reaction will occur at constant speed which will be quite independent of the chemical nature of the subsequent rapid reaction.

If the quantity of halogen per unit volume is a mols at the start and x mols after time t, then

$$-dx/dt = k, \qquad (1)$$

from which, since $x = a$ when $t = 0$,

$$x = a - kt. \qquad (2)$$

The following numbers were obtained in an experiment with diethyl ketone and iodine in aqueous alcoholic solution containing 40 volumes per cent. of alcohol.[1] In the calculation of the values of x in the third column, k is made equal to 0·000059.

Diethyl ketone 0·2532 *mol per litre*, H_2SO_4 0·10 *mol per litre*, *Temp.* 25°.

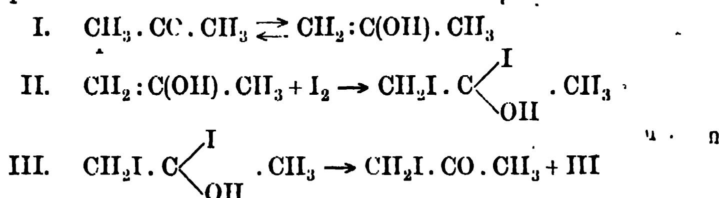
t (*minutes*)	x (*observed*)	x (*calculated*)
0	0·00904	(0·00904)
30	0·00727	0·00727
60	0·00517	0·00550
80	0·00430	0·00432
105	0·00285	0·00284
120	0·00204	0·00196
135	0·00129	0·00108
24 hours	0·00022	—

The reaction evidently slows down a little towards the end, but this is no doubt due to the fact that the second stage is also reversible in character, although under the experimental conditions it may for the sake of simplicity be treated as irreversible.

Reaction between Halogens and Ketones in the absence of an Acid Catalyst. In the absence of an acid, the interaction between

[1] Dawson and Wheatley, *Trans. Chem. Soc.*, 1910, 97, 2048.

iodine and aqueous acetone proceeds very slowly and, at the ordinary temperature, the loss of iodine during the first two or three days is inappreciable. As the reaction proceeds, the velocity increases continuously in consequence of the formation of the gradually increasing quantities of hydriodic acid which accelerates the primary tautomeric change in proportion to the quantity present. We have in this case an example of an auto-accelerated reaction. Although in presence of mineral acid the rate of disappearance of the iodine is only dependent on the speed of formation of the enolic form of acetone, the progress of the auto-accelerated change is determined by the completion of a series of three consecutive changes which may be represented thus:



I. $CH_3.CO.CH_3 \rightleftarrows CH_2:C(OH).CH_3$

II. $CH_2:C(OH).CH_3 + I_2 \rightarrow CH_2I.C\begin{matrix}I\\OH\end{matrix}.CH_3$

III. $CH_2I.C\begin{matrix}I\\OH\end{matrix}.CH_3 \rightarrow CH_2I.CO.CH_3 + HI$

Assuming that reactions II and III are both of high speed relatively to I, then the concentration of the hydriodic acid will, at any moment, be equal to the measured fall in the iodine concentration. If the solution contains c mols of acetone per litre, this being present in large excess compared with the iodine, and x mols of iodine have disappeared after time t, the speed of the primary tautomeric change and therefore that of the complete reaction will be given by

$$dx/dt = kcx \qquad (1)$$

or, if x_1 and x_2 are the values of x after times t_1 and t_2, we obtain on integration

$$k = \frac{1}{c(t_2 - t_1)} \ln \frac{x_2}{x_1} \qquad (2)$$

The following data[1] show that the actual progress of the change is in agreement with the requirements of equation (2). The progress of the reaction was observed by titration of the residual iodine.

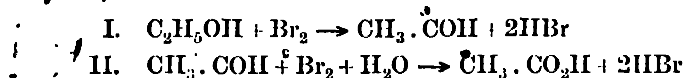
c = 0·272 mol per litre. Original iodine concentration = 0·003976 mol per litre. Temperature 25°.

t (hours)	mols I_2 per litre	x	$k = \frac{1}{c(t-115)} \ln \frac{x}{0{\cdot}000592}$
115	0·003384	0·000592	—
140	0·002758	0·001218	0·1060
163½	0·001616	0·002360	0·1059
170	0·001110	0·002866	0·1054
174	0·000814	0·003162	0·1043

[1] Dawson and Powis, *Trans. Chem. Soc.*, 1912, 101, 1503.

Although these experiments show that the third stage in the reaction proceeds rapidly in comparison with the first, measurements of the electrical conductivity of the solution (the change in which is determined by the hydriodic acid set free) indicate that under certain circumstances there is a very appreciable lag on the part of reaction III as compared with II. When dilute iodine solutions (0·0002 mol per litre) are employed, it is found that the electrical conductivity of the solution increases for some time after the solution has become colourless, and this is no doubt due to the time factor which is involved in the decomposition of the intermediate iodine addition compound.

Oxidation of Alcohol. The oxidation of ethyl alcohol by bromine in dilute aqueous solution[1] affords a further example of a reaction which takes place in consecutive stages, as represented by the formulae



$$\text{I.}\quad C_2H_5OH + Br_2 \rightarrow CH_3.COH + 2HBr$$
$$\text{II.}\quad CH_3.COH + Br_2 + H_2O \rightarrow CH_3.CO_2H + 2HBr$$

Under the same conditions reaction II takes place with much greater speed than I, but, in contrast with the cases previously considered, the velocity of the more rapid reaction is such that it can be measured quite readily[2] under the same conditions as those in which the oxidation of alcohol by bromine has been investigated.

When the ethyl alcohol is present in considerable excess, the speed of the first stage is solely dependent on the concentration of the free bromine, and diminishes continuously as the oxidation proceeds. On the other hand, the speed of the second reaction gradually increases as a result of the increase in the quantity of aldehyde present. When the aldehyde has accumulated to such an extent that the ratio of the alcohol to the aldehyde concentration is equal to the ratio of the velocity coefficients of the reactions II and I, it is evident that both will then proceed at the same rate, so that just as much aldehyde is produced in unit time from the alcohol as is lost by oxidation to acetic acid. This equality in the speeds of the two reactions is obviously dependent on the circumstance that both are of the same 'order' in respect to the bromine. If this were not the case, the relative speeds would vary with the amount of free bromine present at each stage of the reaction. The data obtained by Bugarszky are in satisfactory agreement with this view of the oxidation process.

[1] Bugarszky, *Zeit. physik. Chem.*, 1910, 71, 705.
[2] Bugarszky, *Zeit. physik. Chem.*, 1904, 48, 63.

It is of some interest to note that the action of bromine on ethyl alcohol dissolved in solvents such as carbon tetrachloride, carbon disulphide, and bromobenzene is quite different from that in water solutions, the main product of the reaction being ethyl acetate, as represented by



$$2C_2H_5OH + 2Br_2 = CH_3 . CO_2C_2H_5 + 4HBr.$$

This is also the change which occurs when bromine acts on alcohol-water mixtures containing 80 per cent. alcohol.[1]

Photo-chemical Reactions. Many organic reactions are known which take place only under the influence of light. Such photo-chemical reactions are of two kinds, namely those in which the chemical change is reversed when the light is cut off, and those which are non-reversible. In the case of certain reversible photo-chemical changes, the final state of equilibrium has been found to be dependent on the intensity of the light which acts on the system, and in such cases it may be inferred that the part played by the light rays is not that of an ordinary catalyst.

In their experiments on the photo-chemical combination of hydrogen and chlorine, it was shown by Bunsen and Roscoe[2] that the activity of the rays from a definite source of light is diminished to a much greater extent in passing through a layer of the reacting gases than it is when the light is allowed to pass through an equivalent layer of pure chlorine. Since the absorption due to the admixed hydrogen is negligibly small, it is apparent that the photo-chemical change, which occurs in the mixed gases, is accompanied by the absorption of light energy. This transformation of light energy into chemical energy may be regarded as the distinguishing characteristic of all photo-chemical reactions.

From the data obtained in the experimental investigation of a number of such reactions, it appears that these are in general unimolecular, and are distinguished from reactions which are not light-sensitive by the relatively small influence which an alteration of temperature has on the velocity with which they take place. These facts have led to the view that the absorbed radiant energy is not directly responsible for the chemical change, but that its action consists in a preliminary transformation of the reacting system. This change, which may consist in the intramolecular transformation of the molecules of the light-absorbing substance, or in the formation

[1] Bugarszky, *Zeit. physik. Chem.*, 1901, **38**, 561.
[2] *Ann. Physik*, 1857, **101**, 254.

of molecular complexes which act as reaction nuclei,[1] is then followed by the chemical reaction proper, and if the speed of the latter is relatively very large it is obvious that the rate of formation of the products of the photo-chemical change will be determined by the speed at which the preliminary light change occurs.

If the system in which the photo-chemical reaction occurs is homogeneous, then, according to Nernst,[2] the velocity of the reaction at any moment will be given by the ordinary kinetic equation

$$v = k . a^m . b^n \ldots - k' c^p d^q \ldots$$

in which a, b, ... c, d ... are the concentrations of the reacting substances, m, n, ... p, q ... the number of molecules of the several substances actually involved in the change, and k and k' are the velocity coefficients of the two opposed reactions. The values of k and k' depend on the intensity of the light acting on the system, and for light of the same kind are, in certain cases at any rate, proportional to the intensity. In consequence of absorption, the light intensity varies from point to point of the reaction mixture, with the result that differences in concentration, due to the varying reaction velocities, occur, which can only be equalised by the operation of diffusion or by mechanical mixing. On this account, it is evident that the velocity coefficients which are obtained in any series of experiments can only represent average values, which are influenced by the particular conditions under which the reaction is allowed to take place.

Although in the case of certain non-reversible changes the experimental observations of the rate of change appear to be in satisfactory agreement with the above general equation, it is improbable that this can be regarded as the expression of the fundamental law of photo-kinetics. According to Luther and Weigert,[3] the ordinary dynamic equation is certainly not applicable to reversible photo-chemical changes, and these authors formulate the fundamental law in the following words—'the quantity of a substance, sensitive to light, which undergoes change in a given element of volume per unit of time, is proportional to the light absorbed during the same time by the substance contained in this volume element.'

This quantitative statement is obviously one which refers only to the primary reaction in which the light rays are directly involved, and does not necessarily determine the rate of formation of the final

[1] Cf. Weigert, *Ann. Physik*, 1907 (iv), 24, 243.
[2] *Theoretische Chemie*, Sixth Edition, trans. by H. T. Tizard, 1911.
[3] *Zeit. physik. Chem.*, 1905, 51, 297; 1905, 53, 385.

products of the photo-chemical change, for the rate at which these are produced will be influenced by the relative speeds of the primary light change and any subsequent change or changes of a non-photochemical character. The velocity of these subsequent changes will of course be regulated by the operation of the mass law as expressed in the above general equation (p. 322).

As an example of a reversible photo-chemical change which has been examined in detail, the polymerisation of anthracene will be considered.

Anthracene $\rightleftarrows$ Dianthracene. It was observed by Fritzsche[1] that a benzene solution of anthracene deposits an insoluble polymeric substance when exposed to sunlight. Orndorff and Cameron[2] showed that this substance is dianthracene, which is produced according to $2C_{14}H_{10} \longrightarrow C_{28}H_{20}$. According to Luther and Weigert,[3] the change is reversible, depolymerisation taking place in the absence of light, and in consequence of the opposed reactions a definite state of equilibrium is established when a solution of anthracene (or dianthracene) is exposed to light for a sufficient length of time. The equilibrium condition is dependent on the nature and intensity of the light rays, the nature of the solvent, the temperature, and also the concentration of the solution.

According to the results obtained in experiments with anisole and phenetole solutions at temperatures between 150° and 170°, the depolymerisation of dianthracene is a unimolecular change, the velocity of which is the same in the presence or absence of light. In the dark it proceeds to completion, and its velocity is increased in the ratio of 2·8 : 1 by a rise of temperature of 10° C. On the other hand, the polymerisation of anthracene is dependent on the absorption of light energy, and the velocity with which this change occurs in a given solvent and at a definite temperature is dependent on the nature and intensity of the light, the extent of the surface exposed to the light rays, and the volume of the solution, but is independent of the concentration of the anthracene. As in the case of most photo-chemical reactions, the temperature coefficient is very small, a rise of 10° C. increasing the velocity only in the ratio 1·1 : 1.

In accordance with the above facts, the rate of progress of the photo-chemical change can be represented by the equation

$$dx/dt = k_l - k'x, \qquad (1)$$

[1] *J. prakt. Chem.*, 1866, 101, 337; 1869, 106, 274.
[2] *Amer. Chem. Journ.*, 1893, 17, 658.
[3] *loc. cit.*

in which x is the concentration of the dianthracene at any moment, k' the velocity coefficient for the reaction $C_{28}H_{20} \rightarrow 2C_{14}H_{10}$ which is independent of the incident light, and k_l a quantity characteristic of the reverse change $2C_{14}H_{10} \rightarrow C_{28}H_{20}$ which is, moreover, proportional to the intensity of the absorbed light and the area of the light-absorbing surface, and inversely proportional to the volume of the reaction mixture.

If x_0 is the dianthracene concentration at the commencement and $\xi = k_l/k'$ the corresponding equilibrium value, then, by integration, we obtain

$$k' = \frac{1}{t} ln \frac{\xi - x_0}{\xi - x}, \qquad (2)$$

or, if the solution contains no dianthracene at the start, that is, if $x_0 = 0$, then

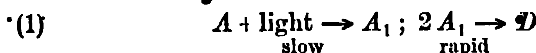
$$k' = \frac{1}{t} ln \frac{\xi}{\xi - x}. \qquad (3)$$

The following table shows the approximate constancy of k' during the progress of the reaction, the data given being the results of an experiment in phenetole solution at 167°.

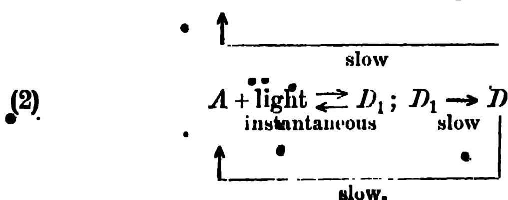
t (*minutes*)	*Anthracene* (*millimols per litre*)	x	$k' . 10^4$
0	37·2	—	—
125	31·8	2·71	32·2
225	29·4	3·90	29·0
370	27·1	5·07	26·4
450	25·5	5·87	28·4
565	24·3	6·45	27·9
790	23·0	7·11	26·3
		ξ = 8·12	

From an examination of all the observations relating to the photochemical change, it may be inferred that dianthracene is not an immediate product of the light action, and Luther and Weigert suppose that intermediate photo-chemically sensitive substances are formed. If this assumption is made, then all the facts can be satisfactorily interpreted on the basis of one or other of the two following schemes, in which A = anthracene, D = dianthracene, A_1 = 'photo-anthracene' and D_1 = 'photo-dianthracene'.

(1) A + light $\rightarrow A_1$; $2A_1 \rightarrow D$
slow rapid



(2) A + light ⇄ D_1 ; $D_1 \rightarrow D$
instantaneous slow



Catalysed Reactions. The velocities of many organic reactions are greatly accelerated by the addition of substances which appear to have no other effect than that of increasing the speed of the change. Acids and bases are the most generally active substances of this character.

The view usually accepted in regard to such catalysed reactions is that the catalyst forms an addition compound with one or other of the original reacting substances, and that the subsequent decomposition of this intermediate substance liberates the catalyst and yields simultaneously the products of the chemical change. Evidence in support of this view has been obtained, not only in the case of the simple catalysts like the acids and bases, but also from a study of reactions in which enzymes play a corresponding part (Part III, chap. 65).

In those cases in which the rôle of the catalyst consists in the formation of intermediate compounds, it is evident that, from a dynamical standpoint, we have to deal with reactions which occur in consecutive stages, and that the phenomena of catalysis will therefore be determined to some extent by the relative speeds of the successive changes in which the catalyst is involved.

Influence of Solvent on Reaction Velocity. The speed of a given reaction not only depends on the active masses of the reacting substances and on the temperature, but varies in a marked manner with the medium in which the reacting substances are dissolved. This solvent influence cannot be referred to catalytic action, for in the case of reversible changes it has been shown that the state of equilibrium differs considerably according to the solvent, whereas a true catalyst, in consequence of the equality of its accelerating effects on the opposed reactions, would be without influence on the final condition of the system.

In the investigations, which have had for their particular goal the elucidation of the influence of the medium, organic reactions have been almost exclusively examined. The data in the following table suffice to show that the influence of the solvent on the speed of chemical change is not determined by the specific character of the solvent, for the order of the solvents, when tabulated according to the velocities of one reaction, is in general quite different from the order obtained when a second reaction is made the basis of comparison.

Under I are given the relative velocities for the reaction between triethylamine and ethyl iodide at 100°,[1] under II corresponding

[1] Menschutkin, *Zeit. physik. Chem.*, 1890, 6, 41.

numbers for the inversion of menthone at 20°,[1] and under III the values for the conversion of the *syn*-form of anisaldoxime into the *anti*-form at 26°.[2]

Solvent.	*I.*	*II.*	*III.*
Methyl alcohol	2·87	1·00	2·07
Ethyl alcohol	2·03	2·60	1·86
Isobutyl alcohol	1·43	4·64	0·96
Allyl alcohol	2·40	0·63	1·56
Benzyl alcohol	7·42	0·37	3·14
Benzene	0·38	—	3·13
Xylene	0·16	—	2·34
Hexane	0·01	—	—

That the influence of the solvent on the speed varies very considerably according to the nature of the reaction is also shown by a comparison of the quantities of the two sets of products, which are formed when two concurrent reactions give rise to the formation of isomeric substances, as in the case of the action of bromine on the homologues of benzene. Bromination experiments have been carried out by Bruner and Vorbrodt,[3] in which the hydrocarbon was diluted with three times its volume of the solvent to be examined and the reaction mixture kept in the dark at 25°. The numbers in the following table, which give the fraction of the total reacting bromine which enters the side-chain, show clearly that the distribution of bromine between side-chain and nucleus is very largely dependent on the solvent, and, since this distribution is determined by the relative velocities of the concurrent reactions, it follows that the influence of the solvent on the speed varies considerably according to the particular chemical change, even when very similar reactions only are considered.

Solvent.	*Toluene.*	*Ethyl benzene.*	*O-Xylene.*	*p-Xylene.*	*m-Xylene.*
CS_2	0·851	1·0	—	0·89	—
CCl_4	0·566	—	0·42	0·63	0·03
C_6H_6	0·355	0·90	—	0·11	0·01
$CHCl_3$	—	0·63	—	—	—
$CH_3.CO_2H$	0·04	0·27	—	—	—
C_6H_5CN	—	0·22	—	—	—
$C_6H_5NO_2$	0·027	0·15	0·026	0·02	—

It has been supposed that the velocity differences are attributable to differences in the ionising power of the various solvents, and in support of this, it has been pointed out that there is, in certain cases, a parallelism between the reaction velocities and dielectric constants of the solvent media. The view that this is the determining factor

[1] Tubandt, *Annalen*, 1907, 354, 259.
[2] Patterson and Montgomerie, *Trans. Chem. Soc.*, 1912, 101, 26.
[3] *Bull. Acad. Sci. Cracow*, 1909, 221.

cannot be entertained very seriously, however, in view of the very different results obtained in the investigation of different reactions.

Although in certain groups of solvents there is some evidence that different reactions are influenced in a uniform manner by the solvent, yet, on the whole, the relationships appear to be so erratic that it seems quite plausible to suppose that the differences are due to the formation of more or less stable compounds between the reacting substances and the solvents in which they are dissolved.

According to van 't Hoff, the velocity of transformation of a substance in different solvents is connected with the solubility of the substance in these media, and evidence in support of such a relationship has been recently obtained by Dimroth.[1]

Further experimental work is necessary, however, before any definite opinion can be expressed as to the general occurrence of such a relationship.

Heterogeneous Reactions. In the foregoing consideration of the kinetics of chemical changes it has been assumed that the system, in which the reacting substances are contained, is homogeneous. A brief reference may now be made to the case where the reacting substances are brought together in different states of aggregation, as in the action of gases on liquids, of liquids on solids or other liquids, &c. In general, such heterogeneous reactions involve a succession of changes, each of which is associated with a time factor, as in the case of the homogeneous consecutive reactions already considered.

In the interaction between liquids and gases or solids, the actual chemical process occurs in the liquid phase, and the chemical change is therefore preceded by a physical process, viz. the dissolution of the gas or solid in the liquid.

The rate at which the final products are formed, as represented by a velocity-time curve, will therefore depend on the relative speeds of the consecutive physical and chemical changes. If the chemical reaction is of high speed, the rate of progress of the change will be determined by the velocity of the dissolution. On the other hand, if the chemical change is relatively slow, and arrangements are made whereby the gas or finely divided solid is maintained in efficient contact with the liquid, e.g. by a suitable shaking apparatus, the liquid will remain in a condition of saturation with respect to the gas or solid in contact with it, and, so far as the succeeding

[1] *Annalen*, 1910, 377, 131.

chemical change is concerned, the active mass of the dissolving substance will be constant. Where the dissolving substance is a gas, it is presumed that the gas pressure is constant, as would be the case if the gas were bubbled in a steady stream through the liquid. Under these circumstances the 'order' of the chemical change will be the determining factor so far as the form of the velocity-time curve is concerned.

Comparatively few organic reactions of the heterogeneous type have been investigated dynamically, but the oxidation of the gaseous hydrocarbons by a solution of potassium permanganate[1] affords a simple example. In the table below are given data obtained in an experiment in which methane was violently agitated with excess of a five per cent. solution of $KMnO_4$.

Period of agitation.	*Volume of methane.*	*Volume change*
5	13·0	—
10	12·7	0·3
15	12·4	0·3
20	12·1	0·3
25	11·7	0·4
30	11·4	0·3

The rate of oxidation is, according to these numbers, constant, and the observed rate of change is probably determined by the velocity of the chemical oxidation process, the solution being maintained in a saturated condition by reason of the intimate contact between the gas and the solution and the consequent rapid rate at which the gas dissolves.

In gas reactions, where the nature and extent of the surface of solids in contact with the reacting gases have been shown to have a large influence on the velocity of the combustion or other chemical change, it is probable that successive processes, which may be grouped under the head of heterogeneous reactions, are frequently involved.

REFERENCES.

Studies in Chemical Dynamics, by J. H. van 't Hoff and E. Cohen. Trans. by T. Ewan. Williams and Norgate, 1906.

Chemical Statics and Dynamics, by J. W. Mellor. Text-books of Physical Chemistry. Longmans, 1904.

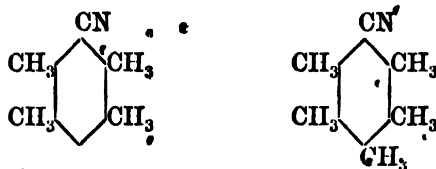
[1] V. Meyer and Saam, *Ber.* 1897, 30, 1935.

CHAPTER V

ABNORMAL REACTIONS

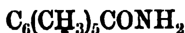
Steric Hindrance. From time to time curious irregularities have been observed in the progress of certain typical reactions. These isolated and scattered examples have now been correlated and traced to one fundamental cause, that of *steric hindrance*. The term is intended to denote the influence exerted on a reacting group by the spatial disposition of neighbouring atoms. The choice of such a term is unfortunate since it connotes a theory which, though applicable as an explanation of some of the abnormal reactions considered in this chapter, is by no means the only underlying cause and possibly in some cases not the cause at all.

As far back as 1872 Hofmann found that dimethylxylidine $(CH_3)_2C_6H_3N(CH_3)_2$, dimethylmesidine $(CH_3)_3C_6H_2N(CH_3)_2$, and pentamethylaminobenzene $(CH_3)_5C_6.NH_2$ give little or no quaternary ammonium compounds when heated with methyl iodide to 150°, and concluded that 'this inability to unite with methyl iodide must depend upon some kind of molecular arrangement'[1] In 1883 Merz and Weith[2] found that perchloro- and perbromo-benzonitrile and hexachloro-α-naphthonitrile cannot be hydrolysed by the usual reagents, and in the following year Hofmann made the same observation in regard to tetramethyl- and pentamethyl-benzonitrile.



During the years 1891 and 1892, in a more extended investigation, Claus and his pupils showed that resistance to hydrolysis is greatly enhanced if one, and still more, if both ortho positions to the cyanogen group are substituted by halogen alkyl or nitro groups.[3]

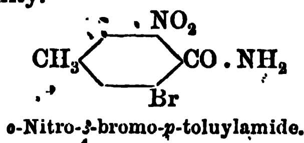
In 1889 Jacobson[4] noticed that pentamethylbenzamide


$$C_6(CH_3)_5CONH_2$$

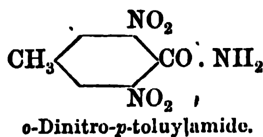
(obtained by the action of aluminium chloride on a mixture of chloroformamide and pentamethylbenzene) completely resists

[1] *Ber.*, 1872, 5, 713, 718; 1875, 8, 61. [2] *Ber.*, 1883, 16, 2886, 2892.
[3] *Annalen*, 1891, 265, 378; 266, 225; 1892, 269, 212 et seq.
[4] *Ber.*, 1889, 22, 1219.

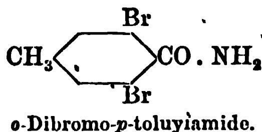
hydrolysis, and Claus[1] again pointed out that, like the nitriles, many diortho-substituted derivatives of *p*-toluylamide exhibit unusual stability.



o-Nitro-*o*-bromo-*p*-toluylamide.

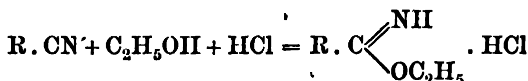


o-Dinitro-*p*-toluylamide.

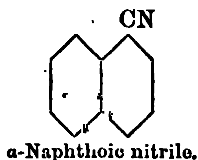


o-Dibromo-*p*-toluylamide.

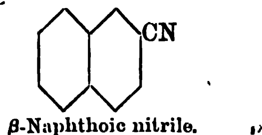
Since then the conditions which determine the hydrolysis of cyanides and amides have been made the subject of more careful study by Sudborough and by Remsen and Reid, and will be referred to again (p. 345). In 1890 Pinner[2] observed similar anomalies in the preparation of imino-ethers from nitriles by the action of alcohol and hydrochloric acid, which usually takes place according to the equation:



Certain ortho-substituted nitriles refused to react. Neither *o*-tolunitrile, 2·4 dimethylbenzonitrile, nor *α*-naphthoic nitrile (which may be regarded as an ortho-substituted compound) give imino ethers, whereas *β*-naphthoic nitrile enters readily into the reaction.

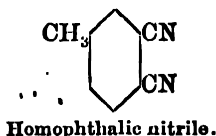


α-Naphthoic nitrile.



β-Naphthoic nitrile.

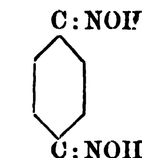
And, again, both cyanogen groups in isophthalic and terephthalic nitrile readily react, whereas in homophthalic nitrile only one cyanogen group forms an imino ether.



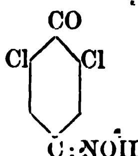
Homophthalic nitrile.

[1] *Annalen*, 1891, **265**, 364; **266**, 223; 1892, **260**, 208.
[2] *Ber.*, 1890, **23**, 2917.

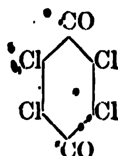
Another series of observations belonging to the same class of phenomena was the subject of a careful study by Kehrmann[1], who found that ortho substitution in the quinones retards or inhibits the formation of oximes. Quinone gives a dioxime, *m*-dichloroquinone yields a monoxime; and chloranil gives none.



Quinonedioxime.



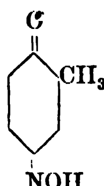
m-Dichloroquinoneoxime.



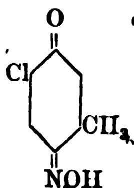
Chloranil.

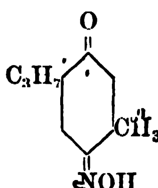
In the case of mono-substituted quinones, such as monochloroquinone and toluquinone, the oxygen which has no ortho substituent is first replaced by the oxime group before the second oxygen reacts.





In the case of para-disubstituted quinones containing a halogen and a methyl group, the oxime group replaces oxygen in the ortho position to the alkyl group. Where two alkyls are present oxygen is first replaced in the ortho position to the smaller group. Examples of this are afforded by *p*-chlorotoluquinone and thymoquinone.



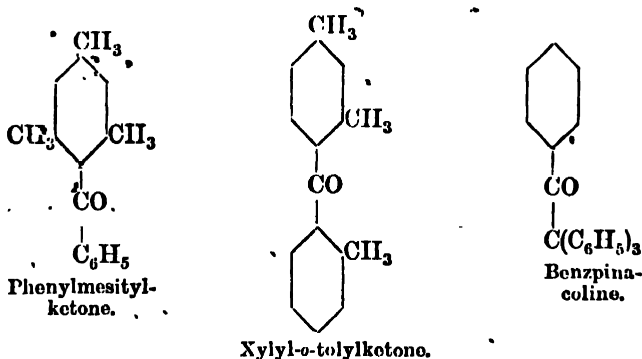


Kehrmann concluded that it is less the nature of the substituents (halogen or alkyl) than their presence in the ortho position to the quinone oxygen which interferes with the reaction.

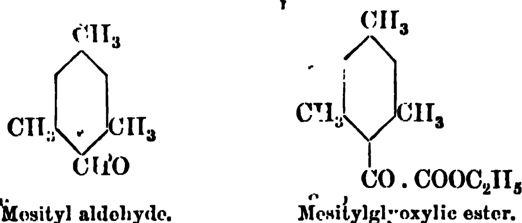
Similar irregularities have frequently been observed in the forma-

[1] *Ber.*, 1888, **21**, 3315; 1890, **23**, 3557; *J. prakt. Chem.*, 1889 (2), **40**, 257; 1890 (2), **42**, 134; see also Nietzki and Schneider, *Ber.*, 1894, **27**, 1431.

tion of oximes from aromatic ketones. Neither phenylmesitylketone, xylyl-*o*-tolylketone nor benzpinacoline react with hydroxylamine.[1]



Many examples of the same kind have been recently brought to light by Baum and V. Meyer.[2] It should, however, be pointed out that the nature of the second radical attached to the ketone group also influences the result, for both mesityl aldehyde and mesitylglyoxylic ester readily form oximes.



From the close analogy existing in structure and mode of formation between the hydrazones and oximes, similar results might be looked for in the action of phenylhydrazine, an anticipation which experience has fully justified. The presence of ortho substituents retard or prevent the reaction in precisely the same way. On the other hand mesitylglyoxylic acid, and especially its dinitro derivative, unite with this reagent.[3]

A further example of interference is afforded by the well-known reaction between aromatic aldehydes and primary aromatic amines, which give rise to benzalanilines. Hantzsch found that the reaction does not occur with symmetrical tribromo- and trinitro-aniline.[4]

[1] Hantzsch, *Ber.*, 1890, **23**, 2773; Smith, *Ber.*, 1891, **24**, 4050; Beckmann and Wegerhoff, *Annalen*, 1889, **252**, 14; Harries and Hübner, *Annalen*, 1897, **296**, 301.
[2] *Ber.*, 1895, **28**, 3207; 1896, **29**, 836, 2564.
[3] *Annalen*, 1891, **264**, 144.
[4] *Ber.*, 1890, **23**, 2776.

Furthermore, the formation of hydrazones of benzaldehyde with ortho-substituted hydrazines, such as *o*-hydrazinebenzoic acid,

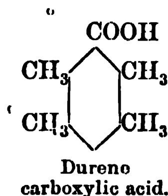


$$C_6H_4(COOH)NHNH_2$$

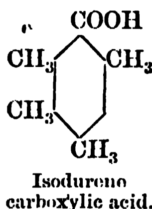
is prevented, whilst the corresponding meta-compound readily combines.

Victor Meyer's Esterification Law. The majority of the foregoing isolated examples of abnormal reactions were known when, in 1894, V. Meyer drew attention to a very remarkable case of interference in the formation of esters, which has found expression in his *esterification law.*

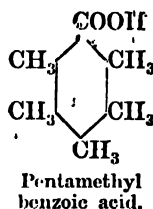
In attempting to prepare the methyl ester of mesitylene carboxylic acid by the action of hydrochloric acid on a mixture of alcohol and acid in the cold, no ester was formed, although the same process produced a nearly theoretical yield in the case of benzoic and its monomethyl, 3:5-dimethyl (mesitylenic acid) and 3:4:6-trimethyl (durylic acid) derivatives.[1] This did not arise from any inability on the part of mesitylene carboxylic acid to form an ester, for it was readily obtained from the silver salt by the action of the alkyl iodide. This observation was followed by the discovery that durene carboxylic, isodurene carboxylic, and pentamethyl benzoic acid, all of which contain methyl groups in both ortho positions to the carboxyl, share the property with mesitylene carboxylic acid in yielding no ester with hydrochloric acid in the cold.



Durene carboxylic acid.



Isodurene carboxylic acid.



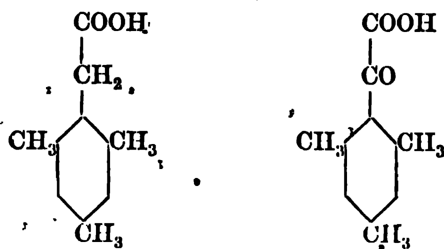
Pentamethyl benzoic acid.

The same thing was found to occur with diortho-substituted chloro-, bromo-, and nitro-benzoic acids, which formed no ester, whilst similar compounds with at least one free ortho position yielded the ester without difficulty.

That the inactivity of the ortho-substituted acids arises from the position occupied by the groups rather than from their chemical nature, is evident from the similar effect produced by both positive

[1] *Ber.*, 1894, **27**, 510, 1580; 1895, **28**, 1255, 2774, 3197; see also Gattermann, *Ber.*, 1899, **32**, 1117.

alkyl and negative halogens and nitro groups. That the interference is further determined by steric conditions seems probable from the behaviour of both mesityl acetic and mesityl glyoxylic acid (in which the carboxyl is removed from the proximity of the two methyl groups), for unlike mesityl carboxylic acid, they readily yield esters.



These preliminary observations led V. Meyer and his pupils to a more elaborate quantitative examination of the phenomenon. In estimating the amount of ester formed at a given temperature they adopted the method of Fischer and Speier, which consists in heating a 1 per cent. solution of the acid in methyl alcohol containing 2 per cent. of hydrogen chloride for two hours in a thermostat. In this way it became possible to determine the relative rate of esterification in cases where the process was not prevented, but merely retarded.

Kellas[1] estimated the relative quantity of ester of ortho-, meta-, and para-isomers of mono-substituted benzoic acids formed at different temperatures, and although he found the rate of esterification to increase with rise of temperature, the ortho compound always yielded the smallest amount of ester. The following examples, which represent the percentage of acid esterified in two hours at 51°, illustrate the point in question:

	CH_3	Cl	Br	I	NO_2
o.	48.3	50.9	43.4	20.5	8.6
m.	77.1	72.0	66.6	57.6	57.1
p.	75.6	70.5	61.0	52.9	57.1

Benzoic acid = 82.5.

The results agree with the velocity constants (K) of esterification which were ascertained by Goldschmidt.[2] The reaction between acid and alcohol is bimolecular, but if the quantity of alcohol is large in proportion to the acid, the former may be regarded as constant in quantity, whilst the influence of the small amount of hydrochloric acid (2 per cent.), which acts the part of a catalyst, is too insignificant to be regarded. The reaction, therefore, resolves itself

[1] *Zeit. phys. Chem.*, 1897, 24, 221. [2] *Ber.*, 1895, 28, 3218.

into a unimolecular one, and the velocity constant may be determined from the usual equation for a unimolecular non-reversible reaction,

$$k = \frac{1}{t} \log \frac{a}{a-x}$$

in which k is the velocity constant, t the time, a the concentration of the acid at the beginning, and x the amount of ester formed in time t. By heating at constant temperature and withdrawing a portion of the mixture at intervals, the quantity of ester formed can be rapidly estimated by titrating the free acid. The following are some of the numbers obtained for k:

	CH_3	Br	NO_2
o.	0·0111	0·0203	0·0028
m.	0·0470	0·0553	0·0296
p.	0·0241	0·0450	0·0261

Benzoic acid = 0·0428.

Attention is drawn to the fact that in both series of determinations the effects of meta- and para-substitution are not equivalent, and the greater esterification values in the case of the meta-compounds points to the existence of other factors in the phenomenon of interference which cannot be disregarded in seeking for a complete explanation. The relative amount of esterification of different diortho acids has also been the subject of a careful study by V. Meyer.[1] He found, for example, that no esterification took place in twelve hours at 0°, or by Fischer and Speier's method in the case of thymotic, *o*-phenylsalicylic, mesitylene carboxylic, and other diortho acids in which both ortho hydrogen atoms are replaced by hydroxyl or methyl groups; but that if hydrochloric acid gas is passed into the boiling alcoholic solution for several hours, the following percentage of ester was formed,

Thymotic acid	23·3
o-Phenylsalicylic „	76·5
Mesitylene carboxylic „	64·5
Pentamethyl benzoic „	70
Durene carboxylic „	60

whereas symmetrical trichloro-, tribromo-, trinitro-, and 2 : 6-dibromobenzoic acids under similar conditions remained unchanged. Van Loon and V. Meyer[2] have also shown that 2-fluoro-6-nitrobenzoic acid gives 2 per cent. of ester on standing for twelve hours at 0°, that is, under conditions which in the case of benzoic acid yield 97 per cent. of ester, whilst V. Meyer found that even the ortho hydrogen atoms in benzoic acid diminish the amount of ester, inasmuch as

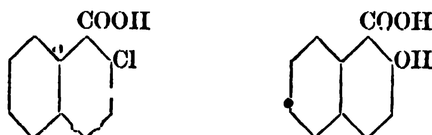
[1] *Ber.*, 1895, 28, 1254. [2] *Ber.*, 1896, 29, 839.

phenylacetic acid is more rapidly esterified than benzoic acid. It would, therefore, appear that whilst hydrogen, fluorine, hydroxyl, and methyl retard esterification, to a greater or less extent, it is only completely arrested by chlorine, bromine, iodine, and nitro groups. V. Meyer draws the conclusion that the atomic weights or size of the groups which prevent esterification in the hot liquid are much larger than those which only produce this effect in the cold.[1]

Retard.	*Prevent.*
H = 1	Cl = 35.4
CH_3 = 15	NO_2 = 46
OH = 17	Br = 80
F = 19	I = 127

This view cannot be strictly maintained; for it has been shown that little, if any, difference is effected by substituting a larger alkyl radical for methyl, and moreover there is little doubt that in spite of its comparatively small atomic weight, the nitro group has a much more powerful effect than the other three halogens of the second column in preventing esterification.[2]

A further interesting observation on the rate of esterification is the effect produced by an adjoining nucleus. From the fact that both β-chloro- and β-hydroxy-α-naphthoic acid cannot be esterified in the cold,



whereas β-chloro- and β-hydroxy-β-naphthoic acid behave like benzoic acid,

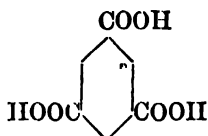


it follows that the CH group of the adjoining nucleus behaves like an ortho substituent.[3]

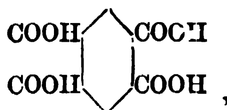
The effect of ortho carboxyl groups on the rate of esterification appears from the behaviour of the polycarboxylic acids to resemble

[1] *Ber.*, 1895, 28, 1260. [2] Kellas, *Zeit. physikal. Chem.*, 1897, 24, 221. [3] *Ber.*, 1895, 28, 125.

generally that of the other groups.[1] Whilst trimesic and pyromellitic acid give a nearly quantitative yield of neutral ester in the cold,

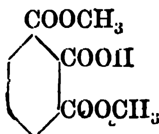


Trimesic acid.

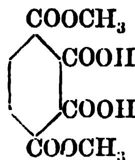


Pyromellitic acid.

homimellitic and prehnitic acid give a dimethyl ester



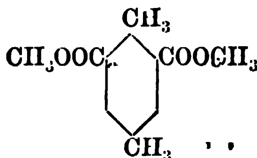
Hemimellitic ester.



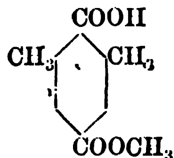
Prehnitic ester.

In boiling alcohol, however, prehnitic acid gives a neutral ester.

The following two dibasic acids give respectively neutral and acid esters:[2]

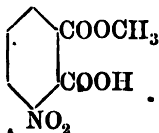


Neutral ester.

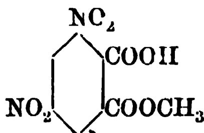


Acid ester.

3-Nitro- and 4 : 6-dinitrophthalic acids yield chiefly monoalkyl esters,



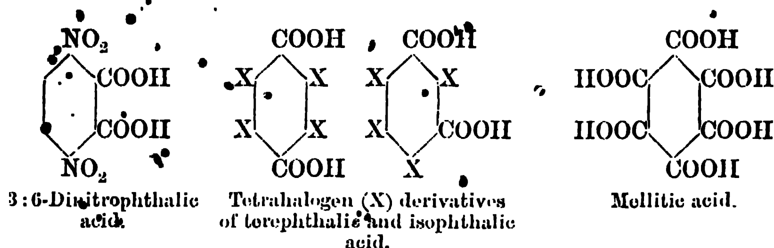
3-Nitrophthalic ester.



4 : 6-Dinitrophthalic ester.

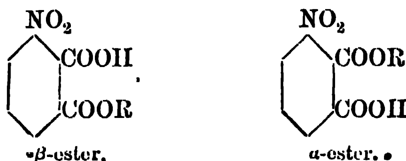
whilst 3 : 6-dinitrophthalic acid, the tetrahalogen derivatives of terphthalic and isophthalic acid and also mellitic acid form no ester at all.[3]

[1] *Ber.* 18?4, 27, 1580.
[2] Ja[illegible] and Weiler, *Ber.*, 1895, 28, 531.
[3] *Ib.* [illegible] 27, 3146; 1895, 28, ?197.



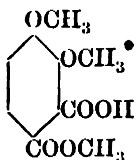
3:6-Dinitrophthalic acid. Tetrahalogen (X) derivatives of terephthalic and isophthalic acid. Mellitic acid.

On the other hand, the tetrahalogen derivatives of phthalic acid and 3:6-dichlorophthalic acid, as well as 3:6-dichloro-2-benzoylbenzoic acid and tetrachloro-2-benzoylbenzoic acid[1] do not obey the esterification law, inasmuch as they form monoalkyl esters. Another exception is the 3-nitrophthalic acid, which, according to Marckwald and McKenzie,[2] forms with amyl alcohol a little α-monoamyl ester in addition to the β-compound, but if the anhydride of the acid is heated with the alcohol, it is the α-ester which is formed. This is true of a large number of alcohols,[3] and has received no explanation.



β-ester. α-ester.

Also hemipinic acid, which forms an acid ester in the first instance,



Hemipinic monomethyl ester.

can be converted by prolonged esterification into the neutral compound.[4]

Among the hydroaromatic acids it is a significant fact that whereas hydromellitic acid forms no ester, the stereoisomeric isohydromellitic acid forms a monoalkyl ester, the difference being no doubt due to a difference in the space configuration of the carboxyl

[1] Graebe, *Ber.*, 1900, 33, 2026.
[2] *Ber.*, 1901, 34, 486.
[3] McKenzie, *Trans. Chem. Soc.*, 1901, 79, 1135; Cohen, Woodroffe and Anderson, *Trans. Chem. Soc.*
[4] Wegscheider, *Monatsh.*, 1895, 16, 137.

groups round the ring. One may suppose that, in the first case, the carboxyl groups are all on the same side of the molecule and, in the second, that one group is reversed (Part II, p. 260).

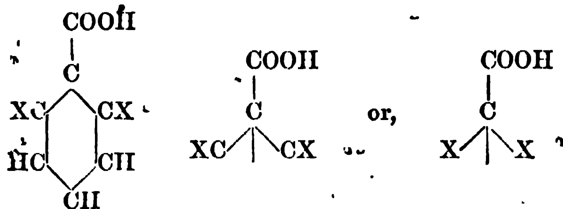
We may conclude then that the carboxyl or carbalkoxyl group, in spite of its atomic weight, resembles the members of the alkyl and hydroxyl series, rather than those of higher atomic weight, seeing that its effect is to retard rather than prevent esterification.

From the results of the above investigation V. Meyer formulated the following law: 'When the hydrogen atoms in the two ortho positions to the carboxyl in a substituted benzoic acid are replaced by radicals, such as Cl, Br, NO_2, CH_3, COOH, an acid results which can only be esterified with difficulty or not at all.'

Although the facts ascertained by V. Meyer and his pupils appear to accord very well with the theory of steric hindrance, it must be remembered that the ester law is only applicable to a particular set of conditions in which a catalyst in the form of hydrogen chloride is used and that the mechanism of the process is still obscure. Rosanoff and Prager[1] have examined the formation of esters of substituted benzoic acids by heating the acid and alcohol together without the addition of a mineral acid and, contrary to Meyer's experience, they find that 'aromatic acids with one or both ortho positions occupied combine with alcohols more slowly although to no less extent than acids otherwise constituted'. Similar results have been obtained by Michael.[2]

It is a significant fact, already mentioned, that whereas 3-nitrophthalic acid when esterified with a catalyst yields mainly the α-ester, the anhydride when heated with an alcohol gives mainly the β-ester.

The Esterification Law applied to Fatty Acids. The interesting results which have been derived from the study of the aromatic acids suggested a similar behaviour on the part of substituted fatty acids which possess a structure analogous to the diortho compounds of the aromatic series.



[1] *Journ. Amer. Chem. Soc.*, 1908, 30, 1895.
[2] *Ber.*, 1909, 42, 310, 317.

In other words, it seemed not unlikely that di- and tri-substituted acetic acids would be influenced by the esterification law. Menschutkin in 1879[1] showed that the rate of esterification of the mono-, di- and tri-methyl acetic acids rapidly decreases in the order given when alcohol and acid are heated together in the absence of hydrogen chloride (autocatalysis[2]). Lichty,[3] using the same method, found that the increase in the number of chlorine atoms facilitated esterification. The subject has received a much more thorough treatment at the hands of Sudborough and his colleagues,[4] who have determined, by the method employed by Goldschmidt, the esterification constants (p. 335) of a long series of substituted acetic acids in presence of hydrochloric acid. The following are the results obtained, in which E stands for the esterification constant for ethyl alcohol at 14·5° and K for the dissociation constant determined by Ostwald and others.

Acid.	Formula.	E.	K.
Acetic	$CH_3.COOH$	3.661	0.00180
Propionic	$CH_2Me.COOH$	3.049	0.00134
Monochloracetic	$CH_2Cl.COOH$	2.132	0.155
Phenylacetic	$CH_2Ph.COOH$	2.068	
Bromacetic	$CH_2Br.COOH$	1.994	0.138
Iodacetic	$CH_2I.COOH$	1.713	0.075
Isobutyric	$CHMe_2.COOH$	1.0196	0.00144
Trimethylacetic	$CMe_3.COOH$	0.0909	0.000978
Dichloracetic	$CHCl_2.COOH$	0.0640	5.14
Diphenylacetic	$CHPh_2.COOH$	0.05586	--
Dibromacetic	$CHBr_2.COOH$	0.0510	—
Trichloracetic	$CCl_3.COOH$	0.0372	121.0
α-Bromisobutyric	$CMe_2Br.COOH$	0.0356	--
αα-Dibromopropionic	$CMeBr_2.COOH$	0.0242	3.3
Tribromacetic	$CBr_3.COOH$	0.01315	--

The experimental evidence clearly indicates that the rate of esterification is retarded in proportion to the number and size of the atoms or groups introduced into the acetic acid molecule, and is independent of the strength of the acid as determined by its dissociation constant. The divergence from Lichty's results, who found that esterification increased with the strength of the acid, may be due, as in the case of the aromatic acids, to the presence of a catalyst. Similar influences therefore affect the esterification of both fatty and aromatic acids. Other contributions to the subject of esterification

[1] *Annalen*, 1879, **195**, 334; **197**, 193.

[2] It also falls off with the greater complexity of the alcohol, the tertiary alcohols combining less readily than the secondary, and the latter less than the primary.

[3] *Amer. Chem. J.*, 1895, **17**, 27; 1896, **18**, 590.

[4] *Trans. Chem. Soc.*, 1899, **75**, 467; see also Gyr, *Ber.*, 1908, **41**, 4308.

have only served to demonstrate the steric effects which underlie the process. One investigation by Sudborough and Lloyd has reference to unsaturated acids of the acrylic series, of the formula $CHX:CY.COOH$ and $CXY:CZ.COOH$,[1] all of which can exist in *cis* and *trans* configurations (Part II, chap. iv). *Cis* acids of both the above formulae are difficult to esterify by Fischer and Speier's method, whilst the corresponding *trans* acids are readily converted into esters. Sudborough and Roberts also found that saturated acids are much more readily esterified than the corresponding unsaturated acids.[2]

A paper[3] by Bone, Sudborough, and Sprankling on the esterification of the mono-esters of the methyl succinic acids 'affords another example of the retardation induced by the successive introduction of methyl groups'. Also, Blaise[4] has shown that in *as*-dimethylsuccinic acid the tertiary carboxyl is more difficult to esterify than the primary group.

The same thing occurs with camphoric and homocamphoric acid in which the tertiary carboxyl remains almost completely unesterified.[5]

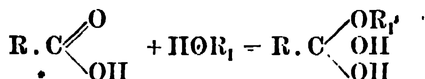




$$\begin{array}{ll} CH_2-C(CH_3).COOH & CH_2-C(CH_3).COOH \\ \quad C(CH_3)_2 & \quad C(CH_3)_2 \\ CH_2-CH.COOR & CH_2-CH.CH_2.COOR \end{array}$$

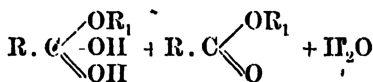
Camphoric ester. Homocamphoric ester.

From what has been already stated of the absence of any relation between the dissociation constants and rate of esterification (p. 341), it is clear that the process is not determined by the presence of free ions, and there are many other facts which point in the same direction. The explanation suggested by Wegscheider[6] assumes that the ester formation is preceded by the addition of a molecule of alcohol and acid,



$$R.C\begin{matrix} \diagup O \\ \diagdown OH \end{matrix} + HOR_1 = R.C\begin{matrix} \diagup OR_1 \\ - OH \\ \diagdown OH \end{matrix}$$

from which water is then removed.



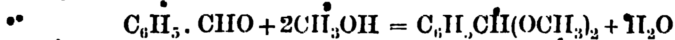
$$R.C\begin{matrix} \diagup OR_1 \\ - OH \\ \diagdown OH \end{matrix} = R.C\begin{matrix} \diagup OR_1 \\ \diagdown O \end{matrix} + H_2O$$

[1] *Trans. Chem. Soc.*, 1898, 73, 81.
[2] *Trans. Chem. Soc.*, 1905, 87, 1840.
[3] *Trans. Chem. Soc.*, 1901, 87, 534.
[4] *Compt. rend.*, 1898, 126, 753.
[5] Haller, *Compt. rend.*, 1889, 109, 68, 112; 1892, 114, 1516.
[6] *Monatsh.*, 1895, 16, 148.

This view finds some confirmation in the fact that whilst benzoic ester forms an additive compound with sodium methoxide, mesitylene carboxylic ester does not.

It is easy to conceive that the presence of large groups or atoms in the neighbourhood of the carboxyl of the acid molecule would interfere with the interaction of the alcohol molecule by preventing the formation of the additive compound.

An apparent contradiction of this view is the formation of acetals (by the action of aldehydes on alcohols in presence of hydrochloric acid) which was studied by E. Fischer and Giebe,[1]



$$C_6H_5.CHO + 2CH_3OH = C_6H_5CH(OCH_3)_2 + H_2O$$

for ortho-substituted aldehydes like 2:5-dichloro- and 2-nitro-3:6-dichloro-benzaldehyde react more readily than the unsubstituted compound itself; but this may be merely an example of steric hindrance neutralized by the specific effect of acidic groups, which, like nitro groups in the hydrolysis of esters (see below), and of ortho-substituted cyanides (p. 345); in the reduction of nitro compounds (p. 350) and in the formation of hydrazones, assist the reaction.

Hydrolysis of Esters. If the esterification law is based on steric hindrance, similar influences might be expected to underlie the rate of ester hydrolysis. Such indeed is the case, although there are notable differences in the character of ester formation and hydrolysis, to which attention will be drawn. The rate of hydrolysis of mono-substituted benzoic esters was examined first by V. Meyer[2] and then more thoroughly by Kellas,[3] who found that substitution in the ortho position hinders the process more than in the meta- or para-position; but whilst methyl in the two latter positions retarded hydrolysis as compared with benzoic ester, the presence of the halogens and still more of the nitro group increased it, so that the absolute rate of hydrolysis of both the mono-halogen and mono-nitro substituted benzoic esters is in many cases greater than that of benzoic ester itself. But as a rule the general effects of ester hydrolysis run parallel with those of esterification, and in most cases the esterification law enables us to predict the result.

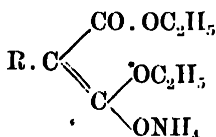
Thus the ortho-substituted esters of α-naphthoic acid are more difficult to hydrolyse than those of the β-compound; in the mono-halogen or mono-nitroterephthalic esters the ester group in the meta position to the substituent is first attacked; the same happens with

[1] *Ber.*, 1898, 31, 545. [2] *Ber.*, 1895, 28, 188.
[3] *Zeit. phys. Chem.*, 1897, 24, 243.

the nitrophthalic esters, in which hydrolysis of the ester group farthest from the nitro group takes precedence. An explanation such as V. Meyer applied to esterification may be repeated here, for the molecule of alkali may form an additive compound with the ester previous to the rupture of the alcohol molecule.

In regard to the aliphatic acids Reicher[1] found that the esters of substituted acetic acids and secondary and tertiary alcohols are more difficult to hydrolyse than those of normal acids and alcohols. Sudborough and Feilmann,[2] from a careful investigation of ester hydrolysis, concluded that two factors were concerned in the process, namely, the configuration of the acid as determined by the proximity of radicals to the carboxyl group and the strength of the acid, and that these two factors may be opposed so that if one is more prominent the effect of the other is concealed.

Hydrolysis of Amides and Acyl Chlorides. The steric influences which retard hydrolysis appear to underlie the formation or non-formation of amides when ammonia acts on esters, and the same phenomenon has been observed in the hydrolysis of ortho-substituted acid chlorides, cyanides, and amides, as well as in the action of alcohols on acid chlorides. Fischer and Dilthey studied the first reaction in the case of the series of alkyl malonic esters,[3] whilst V. Meyer,[4] Sudborough and his collaborators, and also Claus investigated the hydrolysis of acid chlorides, amides, and cyanides of the benzene series. Fischer and Dilthey found that not only did the presence of dialkyl groups in malonic ester retard the formation of amides, but that diethyl and dipropylmalonamide were more slowly hydrolysed than the parent substance.[5] They explain the inactivity of the dialkyl malonic esters on the ground that unlike the monoalkyl derivatives they cannot assume the active tautomeric form represented thus:



From a study of the acid chlorides Sudborough[6] concludes that those, in which either of the ortho positions are substituted, are

[1] *Annalen*, 1885, 228, 257; 1886, 232, 103; 1887, 238, 276.
[2] *Proc. Chem. Soc.*, 1897, 13, 241.
[3] *Ber.*, 1902, 35, 844.
[4] *Ber.*, 1894, 27, 3153.
[5] *Ber.*, 1902, 35, 852.
[6] *Trans. Chem. Soc.*, 1895, 67, 601.

readily decomposed by dilute alkalis, whereas those which have a bromine atom in one ortho position are relatively more stable, but where both ortho-positions are occupied by bromine atoms the compounds are remarkably stable and are only converted into the corresponding sodium salts of the acids by long-continued boiling with an alkali solution.

It has already been mentioned that Claus and his pupils in 1891 and 1892 observed the difficulty with which ortho-substituted benzamides undergo hydrolysis. The subject attracted fresh interest after the discovery of the 'esterification law', and Sudborough, in conjunction with Jackson and Lloyd,[1] submitted the process to a more searching examination. The hydrolysis was effected with 30, 50, or 75 per cent. sulphuric acid at 160°, or at the boiling-point, and a comparison made of the quantities of acid formed in a given time. The results conclusively showed that ortho-substituted derivatives strongly retarded the process, so that under conditions which effected almost complete hydrolysis of 3:5 and 2:4-dibromobenzamide only 11 per cent. of 2:6-dibromo and 4·5 per cent. of 2:4:6-tribromobenzamide were converted. Of the same nature are the constants obtained by Remsen and Reid[2] of the comparative rates of hydrolysis of ortho-, meta-, and para-substituted benzamides in which the retarding effect of the ortho substituent is very evident.

The curious observation made by Fischer[3] that hydroxybenzoic esters and amides (ortho or para) are more easily hydrolysed when the hydrogen of the hydroxyl group is replaced by methyl can scarcely be due to steric influence.

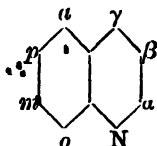
Hydrolysis of Cyanides. That the cyanides should behave like amides on hydrolysis is a natural conclusion which the observations of Claus and others on the hydrolysis of substituted benzonitriles, referred to in the earlier part of the present chapter, have served to confirm. The subject is reopened merely to draw attention to the influence of the nitro group in this reaction, for it is not a little significant that the presence of one, still more of two, nitro groups greatly facilitates hydrolysis. Whilst great difficulty is experienced in hydrolysing *symm*-trimethylbenzonitrile the mono- and dinitro-derivatives may be completely, though slowly, converted into acids.[4] It is clear, therefore, that the nitro group plays a special rôle in

[1] *Trans. Chem. Soc.*, 1895, 67, 601; 1897, 71, 229.
[2] *Amer. Chem. J.*, 1899, 21, 310.
[3] *Ber.*, 1898, 31, 3266.
[4] Küster and Stallberg, *Annalen*, 1894, 278, 207.

modifying steric influences, a fact which also becomes evident in the rate of reduction of nitro compounds (p. 350).

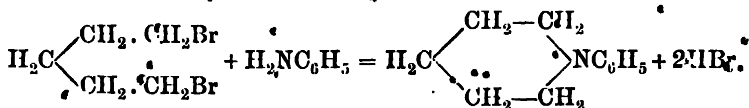
Action of Alcohols on Acid Chlorides. Steric influences also determine the union of acid chlorides with alcohols, and among the series of menthyl esters of disubstituted benzoyl chlorides obtained by the writer and his collaborators,[1] it was invariably found that the diortho compound requires a much higher temperature and more prolonged heating than the other acid chlorides to effect combination with menthol.

Formation of Alkylammonium Iodides. Reference has already been made to Hofmann's observation that certain tertiary aromatic amines refuse to combine with alkyl iodide to form quaternary compounds. The subject was re-investigated by Fischer and Windaus,[2] who showed that it was clearly the effect of steric hindrance. For of the six isomeric xylidines, though they can be converted into tertiary bases by Noelting's method (using methyl iodide and sodium carbonate), it is only the 2 : 6-compound which gives no quaternary ammonium iodide. The same is the case with the different isomeric bromotoluidines and bromoxylidines. Moreover, Friedländer[3] found that 2 : 6-xylidine can, with difficulty, be converted into the tertiary diethyl compound, whilst Effront[4] could only obtain traces of the dimethyl tertiary base with 2-methyl-6-isobutyl toluidine and methyl iodide at 150°. Decker drew attention to the same phenomenon in connection with the *o*- or *a*-substituted quinolines,



which, like the diortho xylidines or bromotoluidines, will not combine with alkyl iodides.

A reaction not very dissimilar from the above is one which was examined by Scholtz and Wassermann.[5] They find that arylamines and *aε*-dibromopentane react to form derivatives of piperidine.



$$H_2C\begin{cases}CH_2.CH_2Br\\CH_2.CH_2Br\end{cases} + H_2NC_6H_5 = H_2C\begin{cases}CH_2—CH_2\\CH_2—CH_2\end{cases}NC_6H_5 + 2HBr.$$

[1] *Trans. Chem. Soc.*, 1906, 89, 1482.
[2] *Ber.*, 1900, 33, 345; 1967; see also v. Braun, *Ber.*, 1913, 46, 3470; 1916, 49, 101; 1917, 50, 1651; 1918, 51, 282.
[3] *Monatsh.*, 1898, 19, 645.
[4] *Ber.*, 1884, 17, 2317.
[5] *Ber.*, 1907, 40, 852.

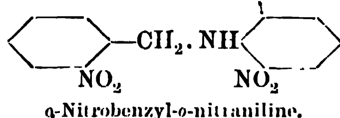
If, however, the amine is substituted in the ortho position, as in o-toluidine and α-naphthylamine, the reaction takes a different course and pentamethylene diamines are formed:



$$RHN.(CH_2)_5.NHR$$

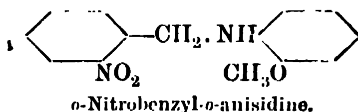
The Alkylation of Bases and Phenols. Decker[1] found that ortho-substituted quinolines will not combine with methyl iodide, but readily react with methyl sulphate. The latter process, however, fails with a number of diortho-substituted bases. In the same way the meta- and para-hydroxybenzoic acids can be alkylated with ease by means of the dialkyl sulphates, but no reaction occurs with salicylic acid or with α- and β-hydroxynaphthoic acids.[2]

Acetylation of Secondary Bases. Paal and Kromschröder[3] have shown that not only does o-nitrobenzyl chloride react with difficulty to form o-nitrobenzyl-o-nitraniline when the m- and p-compounds readily unite, but that the product obtained is proof against acetylation.



o-Nitrobenzyl-o-nitraniline.

Furthermore, of the compounds obtained by combining p-nitrobenzyl chloride with the three isomeric nitranilines, only the o-nitraniline derivative resists the introduction of the acetyl and formyl group. It follows therefore that the ortho-nitro group of the base controls the action, and from the fact that o-nitrobenzyl-o-anisidine gives a formyl derivative, it would seem that this action is determined by the negative character of the group.



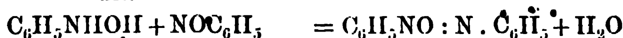
o-Nitrobenzyl-o-anisidine.

Action of Nitrous and Nitric Acid and Diazo-salts on Aromatic Amines. Steric hindrance also[3] appears to modify the action of nitric and nitrous acid and diazo compounds on ortho-substituted secondary and tertiary bases. Thus dimethyl-o-toluidine and o-methoxy-dimethyl aniline, unlike dimethyl aniline, give no nitroso derivatives, although the para position is free. Similarly o-substituted

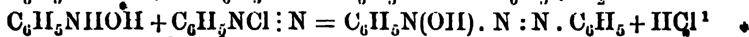
[1] *Ber.*, 1905, 38, 1144.
[2] Cohen and Dudley, *Trans. Chem. Soc.*, 1910, 97, 1739.
[3] *J. prakt. Chem.*, 1896, 54, 265.

dialkyl or acetalkyl anilines give meta- and not para-nitro derivatives. Diazobenzene chloride, which readily forms an aminoazo compound with dimethyl aniline, reacts with difficulty when an ortho-substituted dialkyl aniline is present. In these cases the ortho substituent is supposed to influence the initial formation of an additive compound which is assumed to occur between the nitrogen of the tertiary base and the reagent previous to substitution in the nucleus.

Reactions of Phenylhydroxylamine. Bamberger showed that phenylhydroxylamine unites with nitrosobenzene to form azoxy compounds,[1] and with diazobenzene chloride to form hydroxy diazoamino benzene.



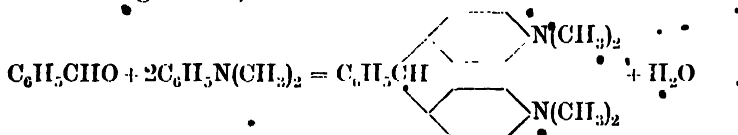
$$C_6H_5NHOH + NOC_6H_5 = C_6H_5NO : N . C_6H_5 + H_2O$$



$$C_6H_5NHOH + C_6H_5NCl : N = C_6H_5N(OH) . N : N . C_6H_5 + HCl^1$$

The two reactions were examined in the case of a number of substituted phenylhydroxylamines containing methyl groups in the nucleus. It was found that where the methyl groups occupied the ortho position to the hydroxylamine group either the speed of the reaction or the amount of the product was greatly reduced.[2] To give one example, when the unsubstituted phenylhydroxylamine reacts with diazobenzene chloride a 99 per cent. yield of the product is obtained; the same reaction with mesitylhydroxylamine gives a 4 per cent. yield.

Action of Benzaldehydes on Aromatic Amines. The same explanation may serve to explain the non-formation of triphenylmethane derivatives when union between aldehydes and *o*-substituted tertiary bases is attempted. The reaction, which occurs according to the following scheme,



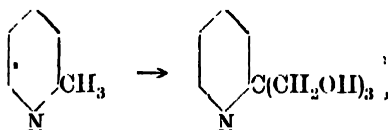
$$C_6H_5CHO + 2C_6H_5N(CH_3)_2 = C_6H_5CH(C_6H_4N(CH_3)_2)_2 + H_2O$$

is effected by attachment of the aldehyde carbon to the para-carbon atom of the amine, and there is no obvious reason why ortho substitution should produce steric hindrance unless some kind of additive compound with the tertiary nitrogen is assumed.

[1] Angeli, *Gazz. Chim.*, 1916, 46, ii, 67.
[2] Bamberger and Rising, *Annalen*, 1901, 316, 257.

If, in place of a tertiary amine, a primary aromatic amine is substituted, it is the *m*-substitution which hinders the reaction. Whilst *o*-toluidine reacts readily with *p*-nitrobenzaldehyde, the *m*-compound does so with difficulty. We must suppose here that the aldehyde carbon attaches itself directly to the para-carbon of the nucleus. That the reactions with primary and tertiary bases should afford so curious a contrast in behaviour is somewhat striking.

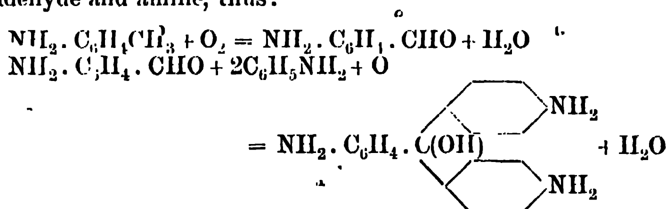
Action of Aldehydes on Pyridine Bases. It is well known that aldehydes combine with *a*- and γ-alkyl pyridine and quinoline bases. Königs[1] found that, if formaldehyde is used, the three hydrogen atoms of the methyl group may all be replaced by carbinol groups thus:



This occurs only if the ortho position to the methyl radical is unsubstituted, otherwise only two carbinol groups replace the hydrogen and this applies to *a*- and γ-methyl quinolines. In the latter case the benzene nucleus may play the part of an ortho substituent and resembles in this respect the effect of the nucleus on the esterification of *a*-naphthoic acid.

Formation of Rosanilines. The difficulty of combining aldehydes with meta-substituted bases reappears in the formation of the rosanilines, in which *p*-toluidine is oxidised in presence of primary aromatic amines, a reaction which in reality resolves itself into a combination of aldehyde and amine, thus:

$$NH_2 . C_6H_4CH_3 + O_2 = NH_2 . C_6H_4 . CHO + H_2O$$
$$NH_2 . C_6H_4 . CHO + 2C_6H_5NH_2 + O$$



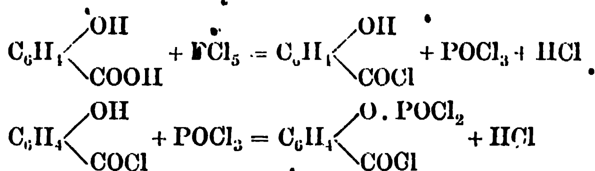
In the example given, both *p*-toluidine and aniline may be replaced by other amines; but Noelting has shown that if, in place of aniline, meta-amines like *m*-toluidine and symm-*m*-xylidine are substituted, the reaction does not take place. The reason from the stereochemical

[1] *Ber.*, 1899, 32, 223, 3599; 1898, 31, 2364.

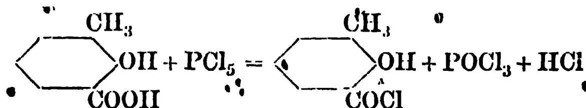
standpoint is clear enough, when we consider that the methyl group in the meta position to the carbon stands in the ortho position to the para-carbon with which the aldehyde group always interacts. The argument might be advanced that rosaniline derivatives, having meta-substituted groups are incapable of existence, but this is met by the fact that indirect methods have been successfully used in their preparation.

Many other examples of steric hindrance might be given, but we shall limit ourselves to two more: the action of phosphorus pentachloride on hydroxy-acids, and of ammonium sulphide on nitro compounds.

Action of Phosphorus Pentachloride on Hydroxy-acids. Anschütz[1] and his pupils have shown that the ordinary course of the reaction between phosphorus pentachloride and hydroxy-acids is usually presented by the following two equations:



If, however, the two ortho positions to the hydroxyl are occupied as in *o*-methylsalicylic acid, the phosphorus oxychloride produces no change in the hydroxyl group.

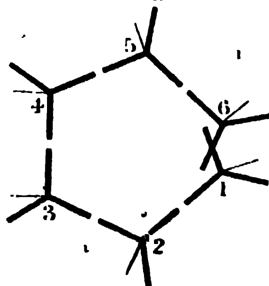


Reduction of Nitro Compounds. The writer, in conjunction with D. McCandlish, studied the action of ammonium sulphide on a variety of substituted nitro derivatives of benzene.[2] It was invariably found that, although the presence of acidic groups facilitates reduction, the nitro group was more slowly attacked by the reducing agent if it occurred in the ortho position to a methyl or ester group, than when present in the meta or para position.

Chain Formation. The subject of steric hindrance would scarcely be complete without some reference to the enormous mass of detailed research which has been accumulated by Bischoff and his collaborators on *chain formation* or conditions affecting the

[1] *Ber.*, 1897, 30, 221.   [2] *Trans. Chem. Soc.*, 1905, 87, 1257.

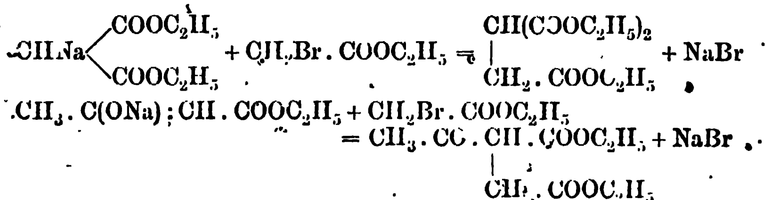
linking of simply constituted compounds. In carrying out these researches he has been guided by what he terms the 'dynamic hypothesis' which is merely an extension of the principle of steric hindrance, and may be explained as follows: as the atoms or groups in a molecule are assumed to be in a state of vibration or oscillation, a reaction will be determined by the amount of free space accorded to the constituent groups undergoing reaction or forming part of the new molecule. The interaction will then be determined not only by the groups adjoining the reacting constituent in each of the molecules, as suggested by V. Meyer, but also by the disposition of the groups in the resulting product. This second condition plays an important rôle, according to Bischoff; for he supposes the atoms in a chain to assume a curved arrangement (p. 179) so that in a chain of 5 or 6 atoms the first and last will be in closer proximity than the first and third or the first and fourth of the chain.



The groups attached to the fifth and sixth atoms of the chain, which are termed the *critical positions*, will therefore be a determining factor equally with those attached to the reacting groups. As in the 'esterification law' the chemical nature of the molecules is not taken into account.

We cannot pretend to review the whole of the materials; but it may be pointed out that steric influences, though not always consistent with Bischoff's hypothesis, are throughout clearly in evidence as factors determining chemical change. A few examples must suffice.

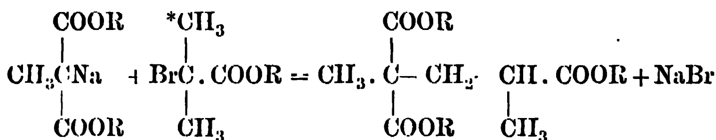
Sodium malonic ester and sodium acetoacetic ester react with α-bromo-fatty esters as follows:



$$CHNa\begin{cases}COOC_2H_5\\COOC_2H_5\end{cases} + CH_2Br.COOC_2H_5 = \begin{array}{l}CH(COOC_2H_5)_2\\|\\CH_2.COOC_2H_5\end{array} + NaBr$$

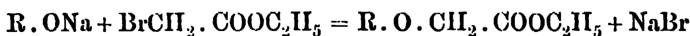
$$CH_3.C(ONa):CH.COOC_2H_5 + CH_2Br.COOC_2H_5 = \begin{array}{l}CH_3.CO.CH.COOC_2H_5\\\qquad\quad|\\\qquad\quad CH_2.COOC_2H_5\end{array} + NaBr$$

In the product of the first reaction the longest uninterrupted chain of carbon atoms is four, in that of the second reaction, five, or in other words, the second reaction involves one of the critical positions, which should manifest itself in a diminished yield. Again, by introducing alkyl groups into the reacting group of the fatty acid or into that of malonic and acetoacetic ester, free vibration of these alkyl groups would be affected and a diminished yield should again follow. The experimental evidence agrees substantially with the results anticipated by the theory. Malonic ester reacts more readily than acetoacetic ester or than its own alkyl or dialkyl derivatives, and moreover it reacts more readily with a normal than with an iso-bromo fatty acid, and finally the two react more readily the shorter the carbon chain in the alkyl groups. For example, if sodium methyl malonic ester and *a*-bromo isobutyric ester are boiled together in alcoholic solution, the reaction proceeds abnormally in the following manner, in which, instead of the *a*-carbon, *C becomes linked to the malonic ester molecule.

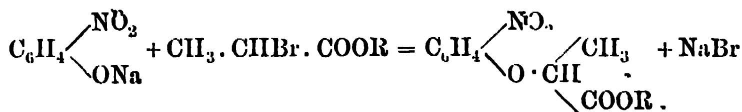


In xylene solution, however, the reaction takes its normal course.

Similar experiments have been carried out with a series of sodium alcoholates and substituted phenates on the one hand and *a*-bromo fatty acids on the other with much the same general result.

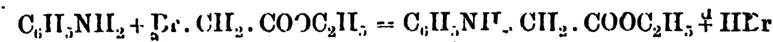


For example, whilst sodium *o*-nitrophenate and *a*-bromopropionic ester combine in a normal fashion,



no reaction occurs with *a*-bromo isobutyric ester.

Another reaction of a similar nature is the union of substituted aromatic amines containing radicals in the nucleus as well as in the amino group with *a* bromo fatty acids according to the equation:



In the last three reactions Bischoff includes the oxygen and nitrogen atoms as part of the chain.

In reviewing the foregoing results it must be admitted that a

strong case has been made out for the principle of steric hindrance. At the same time a fact, which has been frequently emphasized, must not be overlooked, namely, the presence of certain groups which by their chemical nature counteract certain expected changes. In illustration of this, it has been pointed out by Stewart[1] that the formation of bisulphite compounds of ketones is determined by the nature of the radicals attached to the ketone group; that whilst the increase in the size of the hydrocarbon radical retards, the presence of carboxyl facilitates bisulphite formation.

Again, Auwers and Perkin find that, whereas methylacrylic acid condenses readily with sodium malonic ester, dimethylacrylic acid gives a very small yield, and trimethylacrylic acid refuses to react. This may be merely a case of the positive alkyl groups affecting the whole character of the compound and not necessarily one of interference, just as the additive power of olefines for bromine is diminished by the attachment of negative groups, such as carboxyl, ester and phenyl groups, or bromine atoms to the doubly linked carbons. The concurrent influences of position and character of the group are not always easy to differentiate, but for that very reason the conclusion that an apparently anomalous reaction is to be placed to the account of steric influences should be made with caution.

It must be confessed that we are still profoundly ignorant of the change which substituents effect in the character of the molecule as a whole, the causes which determine the rules of orientation, the reason why positive groups like methyl and amino groups facilitate nitration, sulphonation, acetylation by the Friedel-Crafts method,[2] &c., why negative groups assist hydrolysis of cyanides, reduction of nitro groups, acetal formation, &c., and a host of other phenomena of a similar nature. Until clearer views obtain on these subjects it can scarcely be hoped that real progress will be made on the nature of chemical change. The expression 'steric hindrance' meantime affords a useful if not very appropriate title for docketing a number of allied phenomena.

REFERENCES

Der Einfluss der Raumerfüllung der Atomgruppen, by M. Scholtz. Ahrens' *Vorträge*, 1899, 4, 333. Enke, Stuttgart.

Ueber den Einfluss der Kernsubstitution auf die Reaktionsfähigkeit aromatischer Verbindungen, by J. Schmidt. Ahrens' *Vorträge*, 1902, 7, 283. Enke, Stuttgart.

Lehrbuch der Stereochemie, by A. Werner. Fischer, Jena, 1904.

Stereochemistry, by A. W. Stewart. Longmans, 1907.

[1] *Trans. Chem. Soc.*, 1905, 87, 185.

[2] V. Meyer, *Ber.*, 1896, 29, 1413, 2561; Kunckell and Hildebrandt, *Ber.*, 1901, 34, 1826.

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